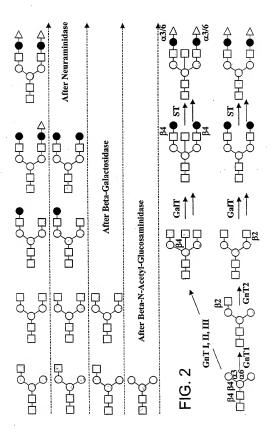


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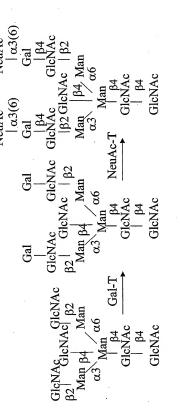
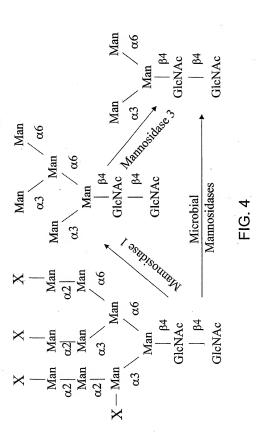


FIG. 3



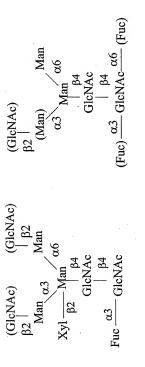
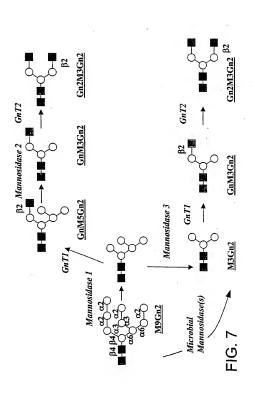
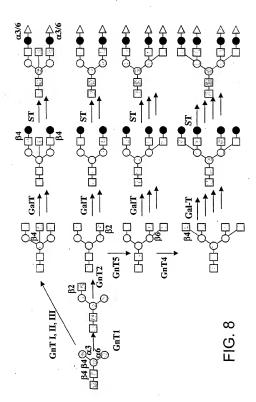
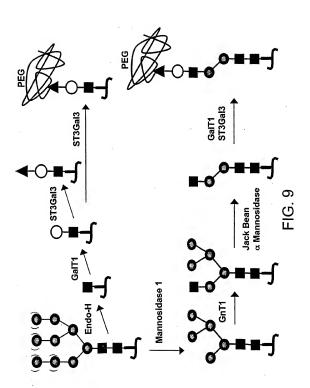


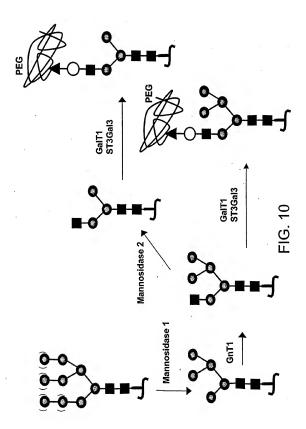
FIG. 6

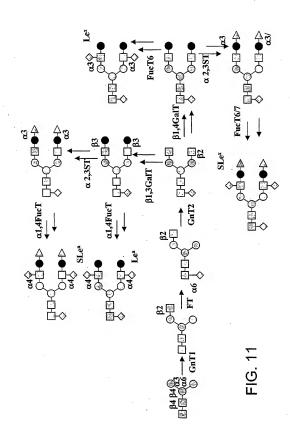


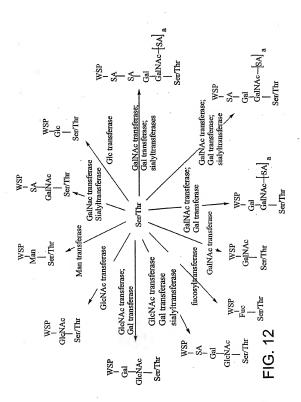




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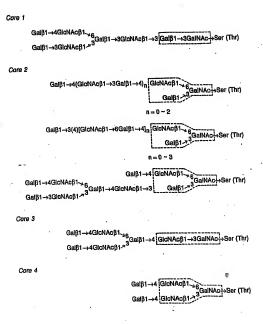
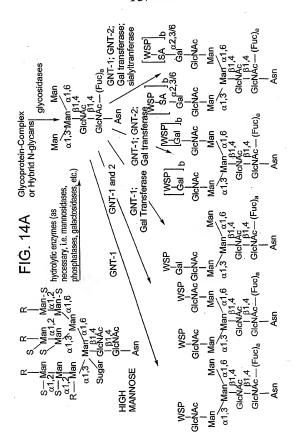
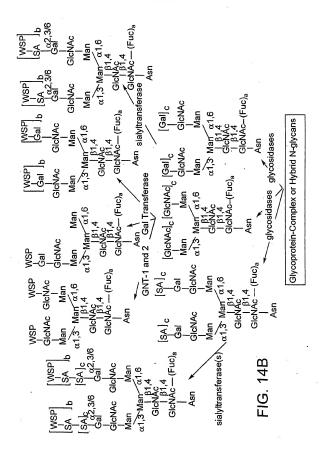


FIG. 13





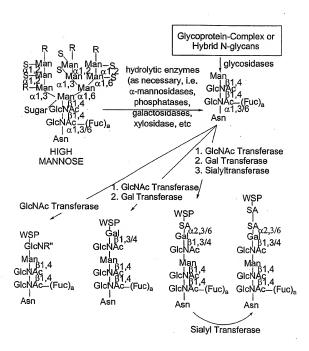


FIG. 15

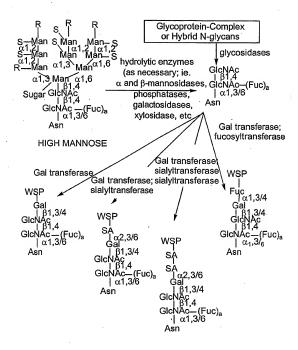


FIG. 16

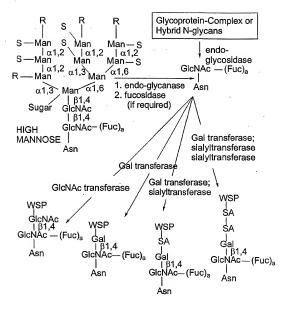
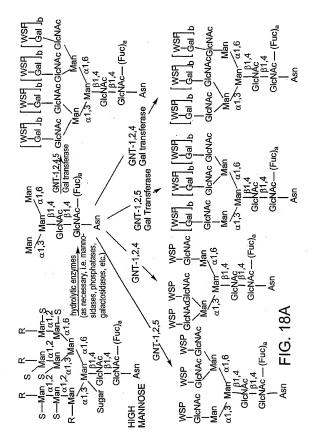
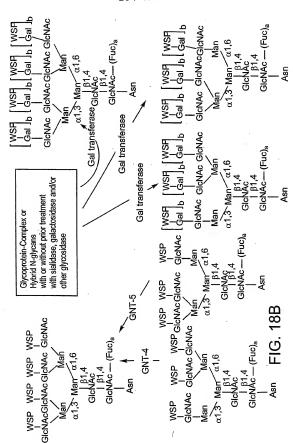
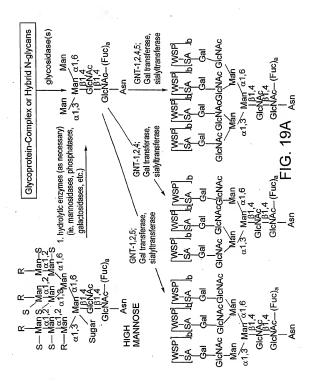
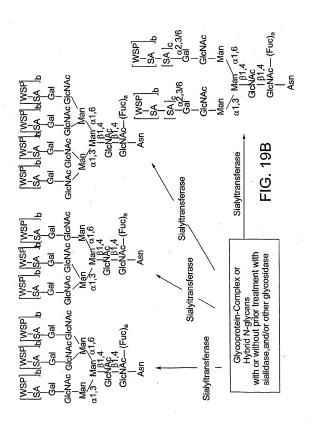


FIG: 17









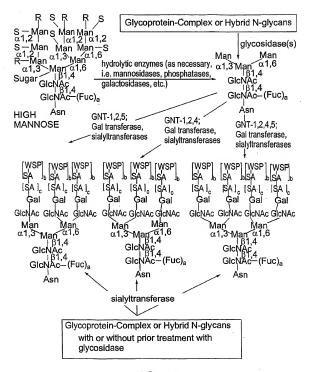
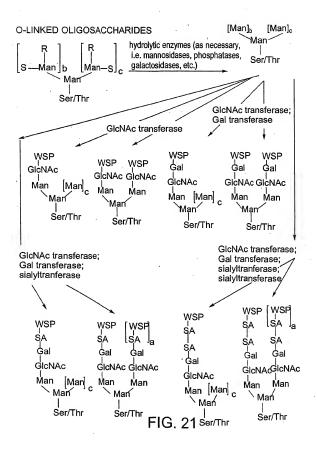
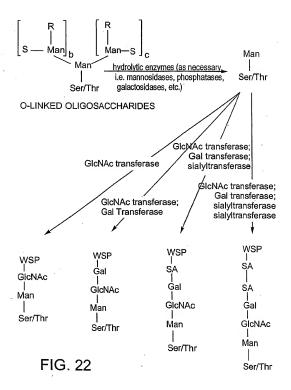
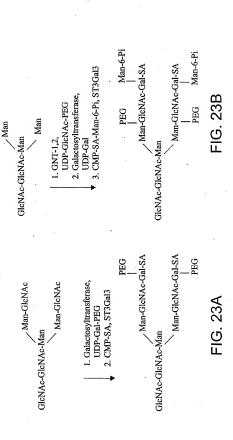


FIG. 20







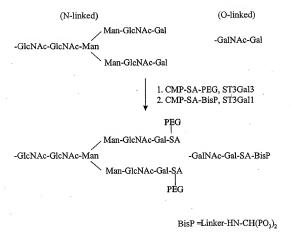
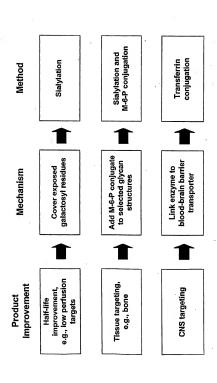


FIG. 23C

FIG. 24



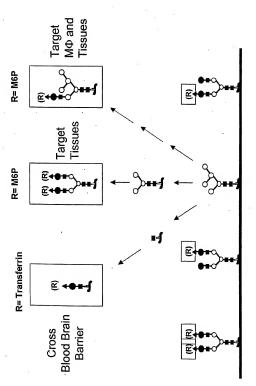
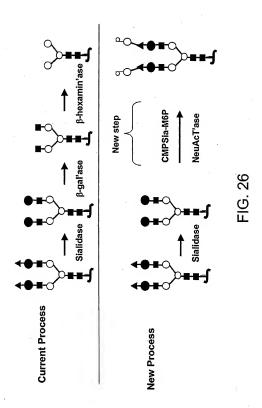


FIG. 25





Sialic acid N-acety/glucosamine Galactose Mannose

FIG. 27

AI-201 - AutoImmune 12AP1/E5 -- Viventia Biotech AI-301 - AutoImmune 1964 -- Aventis AIDS vaccine - ANRS, CIBG, Hesed 20K growth hormone -- AMUR Biomed, Hollis-Eden, Rome, United 28P6/E6 -- Viventia Biotech Biomedical, American Home Products, 3-Hydroxyphthaloyl-beta-lactoglobulin -4-IBB ligand gene therapy -Maxvgen airway receptor ligand -- IC Innovations 64-Cu MAb conjugate TETA-1A3 --AJvW 2 -- Aiinomoto Mallinckrodt Institute of Radiology AK 30 NGF -- Alkermes 64-Cu MAb conjugate TETA-cT84.66 Albuferon -- Human Genome Sciences 64-Cu Trastuzumab TETA conjugate – albumin - Biogen, DSM Anti-Infectives, Genentech Genzyme Transgenics, PPL Therapeutics, A 200 -- Amgen TranXenoGen, Welfide Corp. A10255 - Eli Liliy aldesleukin -- Chiron A1PDX - Hedral Therapeutics alefacept -- Biogen A6 -- Anastrom Alemtuzumab aaAT-III -- Genzyme Allergy therapy -- ALK-Abello/Maxygen, Abciximab -- Centocor ABI,001 - Atlantic BioPharmaceuticals ALK-Abello/RP Scherer allergy vaccines -- Allergy Therapeutics ART-828 - Abbott Alnidofibatide -- Aventis Pasteur Accutin Alnorine - SRC VB VECTOR Actinohivin ALP 242 - Gruenenthal activin -- Biotech Australia, Human Alpha antitrypsin -- Arriva/Hyland Therapeutics, Curis Immuno/ProMetic/Protease Sciences AD 439 - Tanox Alpha-1 antitrypsin - Cutter, Bayer, PPL AD 519 - Tanox Therapeutics, Profile, ZymoGenetics, Adalimumab -- Cambridge Antibody Tech. Arriva Adenocarcinoma vaccine - Biomira - NIS Alpha-1 protease inhibitor -- Genzyme Adenosine deanimase -- Enzond Transgenics, Welfide Corp. Adenosine A2B receptor antagonists --Alpha-galactose fusion protein -Adenosine Therapeutics Immunomedics ADP-001 - Axis Genetics Alpha-galactosidase A -- Research AF 13948 - Affymax Corporation Technologies, Genzyme Afelimomab - Knoll Alpha-glucosidase - Genzyme, Novazyme AFP-SCAN - Immunomedics Alpha-lactalbumin AG 2195 - Corixa Alpha-L-iduronidase -- Transkaryotic agalsidase alfa - Transkaryotic Therapies agalsidase beta -- Genzyme Therapies, BioMarin alteplase -- Genentech AGENT- Antisoma alvircept sudotox - NIH Al 300 - AutoImmune ALX-0600, a GLP-2 agonist -- NPS Allelix Al-101 - Teva Corp. Al-102 - Teva

ALX1-11 -sNPS Pharmaceuticals Molecular Evolution Alzheimer's disease gene therapy Anti-angiogenesis monoclonal antibodies --AM-133 -- AMRAD KS Biomedix/Schering AG Amb a 1 immunostim conj. -- Dynavax Anti-B4 MAb-DC1 conjugate -- ImmunoGen AMD 3100 - AnorMED -- NIS Anti-B7 antibody PRIMATIZED -- IDEC AMD 3465 - AnorMED -- NIS AMD 3465 - AnorMED -- NIS Anti-B7-1 MAb 16-10A1 Anti-R7-1 MAb 1G10 AMD Fab -- Genentech Amediplase - Menarini, Novartis Anti-B7-2 MAb GL-1 Anti-B7-2-gelonin immunotoxin -AM-F9 Amoebiasis vaccine Antibacterials/antifungals --Diversa/IntraBiotics Amphiregulin -- Octagene Anti-beta-amyloid monoclonal antibodies -anakinra -- Amgen Cambridge Antibody Tech., Wyeth-Ayerst analgesic -- Nobex Anti-BLvS antibodies -- Cambridge ancestim -- Amgen Antibody Tech. /Human Genome Sciences AnergiX.RA - Corixa, Organon Antibody-drug conjugates -- Seattle Angiocidin -- InKine Genetics/Eos angiogenesis inhibitors -- ILEX Anti-C5 MAb BB5-1 -- Alexion AngioMab - Antisoma Angiopoietins -- Regeneron/Procter & Anti-C5 MAb N19-8 -- Alexion Anti-C8 MAb anticancer cytokines - BioPulse angiostatin -- EntreMed Angiostatin/endostatin gene therapy -anticancer matrix - Telios Integra Anticancer monoclonal antibodies - ARIUS. Genetix Pharmaceuticals angiotensin-II. topical -- Maret **Immunex** anticancer peptides - Maxygen, Micrologix Anthrax -- EluSys Therapeutics/US Army Medical Research Institute Anticancer prodrug Tech. -- Alexion Anthrax vaccine Antibody Technologies Anti platelet-derived growth factor D human anticancer Troy-Bodies - Affite -- Affitech anticancer vaccine -- NIH monoclonal antibodies - CuraGen Anti-17-1A MAb 3622W94 -anticancers -- Epimmune Anti-CCR5/CXCR4 sheep MAb -- KS GlaxoSmithKline Anti-2C4 MAb -- Genentech Biomedix Holdings anti-4-1BB monoclonal antibodies -- Bristol- Anti-CD11a MAb KBA --Myers Squibb Anti-CD11a MAb M17 Anti-Adhesion Platform Tech. -- Cytovax Anti-CD11a MAb TA-3 -Anti-adipocyte MAb -- Cambridge Antibody Anti-CD11a MAb WT.1 --Tech./ObeSvs Anti-CD11b MAb -- Pharmacia antiallergics -- Maxygen Anti-CD11b MAb LM2 antiallergy vaccine -- Acambis Anti-CD154 MAb -- Biogen

Anti-CD16-anti-CD30 MAb -- Biotest

Anti-alpha-4-integrin MAb

Anti-CD18 MAb -- Pharmacia Anti-CD4 MAb - Centocor, IDEC Pharmaceuticals, Xenova Group Anti-CD19 MAb B43 -Anti-CD19 MAb -liposomal sodium butyrate Anti-CD4 MAb 16H5 Anti-CD4 MAb 4162W94 - GlaxoSmithKline conjugate -Anti-CD4 MAb B-F5 -- Diaclone Anti-CD147 Anti-CD19 MAb-saporin conjugate -Anti-CD4 MAb GK1-5 Anti-CD19-dsFv-PE38-immunotoxin -Anti-CD4 MAb KT6 Anti-CD4 MAb OX38 Anti-CD2 MAb 12-15 --Anti-CD4 MAb PAP conjugate -- Bristol-Anti-CD2 MAb B-E2 -- Diaclone Myers Squibb Anti-CD2 MAb OX34 -Anti-CD4 MAb RIB 5-2 Anti-CD2 MAb OX54 -Anti-CD4 MAb W3/25 Anti-CD2 MAb OX55 -Anti-CD4 MAb YTA 3.1.2 Anti-CD2 MAb RM2-1 Anti-CD4 MAb YTS 177-9 Anti-CD2 MAb RM2-2 Anti-CD40 ligand MAb 5c8 -- Biogen Anti-CD2 MAb RM2-4 Anti-CD40 MAb Anti-CD20 MAb BCA B20 Anti-CD20-anti-Fc alpha RI bispecific MAb -Anti-CD40 MAb 5D12 - Tanox Anti-CD44 MAb A3D8 Medarex. Tenovus Anti-CD22 MAb-saporin-6 complex -Anti-CD44 MAb GKWA3 Anti-CD44 MAb IM7 Anti-CD3 immunotoxin -Anti-CD3 MAb 145-2C11 -- Pharming Anti-CD44 MAb KM81 Anti-CD44 variant monoclonal antibodies --Anti-CD3 MAb CD4lgG conjugate --Corixa/Hebrew University Genentech Anti-CD3 MAb humanised - Protein Design, Anti-CD45 MAb BC8-I-131 Anti-CD45RB MAb RW Johnson Anti-CD48 MAb HuLy-m3 Anti-CD3 MAb WT32 Anti-CD3 MAb-ricin-chain-A conjugate -Anti-CD48 MAb WM-63 Anti-CD3 MAb-xanthine-oxidase conjugate Anti-CD5 MAb -- Becton Dickinson Anti-CD5 MAb OX19 Anti-CD30 MAb BerH2 -- Medac Anti-CD6 MAb Anti-CD7 MAb-PAP conjugate Anti-CD30 MAb-saporin coniugate Anti-CD7 MAb-ricin-chain-A conjugate Anti-CD30-scFv-ETA'-immunotoxin Anti-CD8 MAb - Amerimmune, Cvtodyn, Anti-CD38 MAb AT13/5 Anti-CD38 MAb-saporin conjugate Becton Dickinson Anti-CD3-anti-CD19 bispecific MAb Anti-CD8 MAb 2-43 Anti-CD3-anti-EGFR MAb Anti-CD8 MAb OX8 Anti-CD3-anti-interleukin-2-receptor MAb Anti-CD80 MAb P16C10 -- IDEC Anti-CD80 MAb P7C10 -- ID Vaccine Anti-CD3-anti-MOv18 MAb -- Centocor Anti-CD3-anti-SCLC bispecific MAb Anti-CD8-idarubicin conjugate Anti-CD4 idiotype vaccine Anti-CEA MAb CE-25

Anti-CFA MAb MN 14 - Immunomedics

WO 2004/033651 PCT/US2003/031974

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Anti-heparanase human monocional Anti-CEA MAb MN14-PE40 conjugate antibodies -- Oxford Immunomedics Anti-CEA MAb T84,66-interleukin-2 Glycosciences/Medarex Anti-hepatitis C virus human monoclonal conjugate antibodies -- XTL Biopharmaceuticals Anti-CEA sheep MAb -- KS Biomedix Anti-HER-2 antibody gene therapy Holdinas Anti-herpes antibody - Epicyte Anti-cell surface monoclonal antibodies --Anti-HIV antibody - Epicyte Cambridge Antibody Tech. /Pharmacia anti-HIV catalytic antibody -- Hesed Biomed Anti-c-erbB2-anti-CD3 bifunctional MAb -anti-HIV fusion protein -- Idun Otsuka anti-HIV proteins -- Cangene Anti-CMV MAb -- Scotgen Anti-HM1-24 MAb -- Chugai Anti-complement Anti-hR3 MAb Anti-CTLA-4 MAb Anti-Human-Carcinoma-Antigen MAb --Anti-EGFR catalytic antibody -- Hesed Riomed Epicyte Anti-ICAM-1 MAb -- Boehringer Ingelheim anti-FGFR immunotoxin -- IVAX Anti-ICAM-1 MAb 1A-29 - Pharmacia Anti-EGFR MAb -- Abgenix Anti-ICAM-1 MAb HA58 Anti-EGFR MAb 528 Anti-EGFR MAb KSB 107 -- KS Biomedix Anti-ICAM-1 MAb YN1/1.7.4 Anti-ICAM-3 MAb ICM3 -- ICOS Anti-EGFR MAb-DM1 conjugate --Anti-idiotype breast cancer vaccine 11D10 ImmunoGen Anti-idiotype breast cancer vaccine Anti-FGFR MAb-LA1 -ACA14C5 -Anti-EGFR sheep MAb -- KS Biomedix Anti-idiotype cancer vaccine -- ImClone Anti-FAP MAb F19-I-131 Systems/Merck KGaA ImClone, Viventia Anti-Fas IgM MAb CH11 Anti-Fas MAb Jo2 Biotech Anti-idiotype cancer vaccine 1A7 -- Titan Anti-Fas MAb RK-8 Anti-Fit-1 monoclonal antibodies -- ImClone Anti-idiotype cancer vaccine 3H1 -- Titan Anti-idiotype cancer vaccine TriAb -- Titan Anti-fungal peptides -- State University of Anti-idiotype Chlamydia trachomatis New York antifungal tripeptides - BTG vaccine Anti-ganglioside GD2 antibody-interleukin-2 Anti-idiotype colorectal cancer vaccine --Novartis fusion protein -- Lexigen Anti-idiotype colorectal cancer vaccine --Anti-GM2 MAb -- Kyowa Anti-GM-CSF receptor monoclonal Onvvax Anti-idiotype melanoma vaccine -- IDEC antibodies -- AMRAD Anti-gp130 MAb -- Tosoh **Pharmaceuticals** Anti-HCA monoclonal antibodies --Anti-idiotype ovarian cancer vaccine ACA AltaRex/Epigen Anti-hCG antibodies -- Abgenix/AVI Anti-idiotype ovarian cancer vaccine AR54 -- AltaRex BioPharma

Anti-L-selectin monoclonal antibodies --Anti-idiotype ovarian cancer vaccine CA-Protein Design Labs, Abgenix, Stanford 125 - AltaRex, Biomira Anti-IgE catalytic antibody - Hesed Biomed University Anti-MBL monoclonal antibodies --Anti-laE MAb E26 -- Genentech Alexion/Brigham and Women's Hospital Anti-IGF-1 MAb Anti-MHC monoclonal antibodies anti-inflammatory -- GeneMax Anti-MIF antibody humanised - IDEC, anti-inflammatory peptide -- BTG Cytokine PharmaSciences anti-integrin peptides -- Burnha Anti-interferon-alpha-receptor MAb 64G12 -- Anti-MRSA/VRSA sheep MAb -- KS Biomedix Holdings Pharma Pacific Management Anti-interferon-gamma MAb -- Protein Anti-mu MAb -- Novartis Anti-MUC-1 MAb Design Labs Anti-interferon-gamma polyclonal antibody - Anti-MUC 18 - Advanced Biotherapy Anti-Nogo-A MAb IN1 Anti-nuclear autoantibodies -- Procyon Anti-interleukin-10 MAb -Anti-ovarian cancer monoclonal antibodies -Anti-interleukin-12 MAb -Anti-interleukin-1-beta polyclonal antibody -- - Dompe Anti-p185 monoclonal antibodies R&D Systems Anti-p43 MAb Anti-interleukin-2 receptor MAb 2A3 Antiparasitic vaccines Anti-interleukin-2 receptor MAb 33B3-1 --Anti-PDGF/bFGF sheep MAb -- KS Immunotech Biomedix Anti-interleukin-2 receptor MAb ART-18 Anti-properdin monoclonal antibodies --Anti-interleukin-2 receptor MAb LO-Tact-1 Abgenix/Gliatech Anti-interleukin-2 receptor MAb Mikbeta1 Anti-PSMA (prostrate specific membrane Anti-interleukin-2 receptor MAb NDS61 Anti-interleukin-4 MAb 11B11 antigen) Anti-interleukin-5 MAb -- Wallace Anti-PSMA MAb J591 -- BZL Biologics Anti-Rev MAb gene therapy -Laboratories Anti-RSV antibodies - Epicyte, Intracell Anti-interleukin-6 MAb - Centocor, Anti-RSV monoclonal antibodies --Diaclone, Pharmadigm Anti-interleukin-8 MAb -- Abgenix Medarex/MedImmune, Applied Molecular Evolution/MedImmune Anti-interleukin-8 MAb - Xenotech Anti-RSV MAb, inhalation --Anti-. II 1 MAh Anti-Klebsiella sheep MAb -- KS Biomedix Alkermes/MedImmune Anti-RT gene therapy Holdings Antisense K-ras RNA gene therapy Anti-Laminin receptor MAb-liposomal Anti-SF-25 MAb doxorubicin conjugate Anti-LCG MAb -- Cytoclonal Anti-sperm antibody -- Epicyte Anti-Tac(Fv)-PE38 conjugate Anti-lipopolysaccharide MAb -- VitaResc Anti-TAPA/CD81 MAb AMP1

Anti-tat gene therapy

AOP-RANTES -- Senetek

Anti-TCR-alphabeta MAb H57-597 Anti-TCR-alphabeta MAb R73 Anti-tenascin MAb BC-4-I-131 Anti-TGF-beta human monoclonal antibodies -- Cambridge Antibody Tech., Genzyme Anti-TGF-beta MAb 2G7 -- Genentech Antithrombin III -- Genzyme Transgenics, Aventis, Bayer, Behringwerke, CSL, Myriad Anti-Thv1 MAb Anti-Thv1.1 MAb Anti-tissue factor/factor VIIA sheep MAb --KS Biomedix Anti-TNF monoclonal antibodies -Centocor, Chiron, Peptech, Pharacia, Anti-TNF sheep MAb - KS Biomedix Holdings Anti-TNFalpha MAb -- Genzyme Anti-TNFalpha MAb B-C7 -- Diaclone Anti-tooth decay MAb -- Planet BioTech. Anti-TRAIL receptor-1 MAb -- Takeda Antitumour RNases -- NIH Anti-VCAM MAb 2A2 - Alexion Anti-VCAM MAb 3F4 - Alexion Anti-VCAM-1 MAb Anti-VEC MAb -- ImClone Anti-VEGF MAb -- Genentech Anti-VEGE MAb 2C3 Anti-VEGF sheep MAb -- KS Biomedix Holdings Anti-VLA-4 MAb HP1/2 -- Biogen Anti-VI A-4 MAh PS/2 Anti-VLA-4 MAb R1-2 Anti-VLA-4 MAb TA-2 Anti-VAP-1 human MAb Anti-VRE sheep MAb -- KS Biomedix Holdings ANUP -- TranXenoGen ANUP-1 -- Pharis

Apan-CH - Praecis Pharmaceuticals APC-8024 -- Demegen ApoA-1 -- Milano, Pharmacia Apogen -- Alexion apolipoprotein A1 -- Avanir Apolipoprotein E -- Bio-Tech. General Applaggin - Biogen aprotinin -- ProdiGene APT-070C - AdProTech AR 177 -- Aronex Pharmaceuticals AR 209 -- Aronex Pharmaceuticals, **Antigenics** AR545C ARGENT gene delivery systems - ARIAD Arresten ART-123 -- Asahi Kasei arvisulfatase B -- BioMarin Arylsulfatase B, Recombinant human --**BioMarin** AS 1051 -- Aiinomoto ASI-BCL -- Intracell Asparaginase - Merck ATL-101 - Alizyme Atrial natriuretic peptide -- Pharis Aurintricarboxylic acid-high molecular weiaht Autoimmune disorders -- GPC Biotech/MorphoSvs Autoimmune disorders and transplant rejection -- Bristol-Myers Squibb/Genzyme Tra Autoimmune disorders/cancer --Abgenix/Chiron, CuraGen Autotaxin -Avicidin - NeoRx axogenesis factor-1 -- Boston Life Sciences Axokine -- Regeneron B cell lymphoma vaccine -- Biomira B7-1 gene therapy -BABS proteins -- Chiron

RMP 2 -- Genetics Institute/Medtronic-BAM-002 -- Novelos Therapeutics Sofamor Danek, Genetics Institute/ Basiliximab (anti CD25 MAb) -- Novartis Collagenesis, Genetics Bay-16-9996 -- Bayer Institute/Yamanouch Bay-39-9437 -- Bayer BMP 2 gene therapy Bay-50-4798 -- Bayer BMP 52 -- Aventis Pasteur, Biopharm BB-10153 -- British Biotech RMP-2 -- Genetics Institute BBT-001 -- Bolder BioTech. BMS 182248 -- Bristol-Myers Squibb BBT-002 -- Bolder BioTech. BMS 202448 - Bristol-Myers Squibb BRT-003 -- Bolder BioTech. bone growth factors -- IsoTis BBT-004 -- Bolder BioTech. BPC-15 -- Pfizer BRT-005 -- Bolder BioTech. brain natriuretic peptide -BBT-006 -- Bolder BioTech. Breast cancer -- Oxford BBT-007 -- Bolder BioTech. GlycoSciences/Medarex BCH-2763 -- Shire Breast cancer vaccine -- Therion Biologics. BCSF -- Millenium Biologix BDNF -- Regeneron - Amgen Oregon Becaplermin -- Johnson & Johnson, Chiron BSSL -- PPL Therapeutics BST-2001 – BioStratum Bectumomab - Immunomedics BST-3002 -- BioStratum Beriplast -- Aventis BTI 322 -Beta-adrenergic receptor gene therapy -butvrvlcholinesterase - Shire University of Arkansas C 6822 -- COR Therapeutics bFGF -- Scios C1 esterase inhibitor -- Pharming BI 51013 - Behringwerke AG C3d adjuvant -- AdProTech BIBH 1 -- Boehringer Ingelheim CAB-2.1 -- Millennium BIM-23190 - Beaufour-Ipsen calcitonin - Inhale Therapeutics Systems, birch pollen immunotherapy -- Pharmacia Aventis, Genetronics, TranXenoGen. bispecific fusion proteins -- NIH Unigene, Rhone Poulenc Rohrer Bispecific MAb 2B1 - Chiron calcitonin -- oral - Nobex, Emisphere. Bitistatin Pharmaceutical Discovery BIWA 4 -- Boehringer Ingelheim Calcitonin gene-related peptide -- Asahi blood substitute - Northfield, Baxter Intl. BI P-25 -- Biomira Kasei - Unigene BLS-0597 -- Boston Life Sciences calcitonin, human -- Suntory calcitonin, nasal - Novartis, Unigene BLvS -- Human Genome Sciences calcitonin, Panoderm - Elan BLvS radiolabelled -- Human Genome calcitonin, Peptitrol -- Shire Sciences calcitonin, salmon -- Therapicon BM 06021 -- Boehringer Mannheim calin -- Biopharm BM-202 -- BioMarin Calphobindin I BM-301 -- BioMarin calphobindin I -- Kowa BM-301 -- BioMarin calreticulin -- NYU BM-302 -- BioMarin

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CD4 fusion toxin -- Senetek Campath-1G CD4 IgG -- Genentech Campath-1M CD4 receptor antagonists -cancer therapy -- Cangene Pharmacopeia/Progenics cancer vaccine - Aixlie, Aventis Pasteur, CD4 soluble -- Progenics Center of Molecular Immunology, YM CD4. soluble -- Genzyme Transgenics BioSciences, Cytos, Genzyme, CD40 ligand -- Immunex Transgenics, Globelmmune, Igeneon, CD4-ricin chain A -- Genentech ImClone, Virogenetics, InterCell, Iomai, CD59 gene therapy -- Alexion Jenner Biotherapies, Memorial Sloan-Kettering Cancer Center, Sydney Kimmel CD8 TIL cell therapy -- Aventis Pasteur CD8. soluble -- Avidex Cancer Center, Novavax, Protein CD95 ligand -- Roche Sciences, Argonex, SIGA CDP 571 -- Celltech Cancer vaccine ALVAC-CEA B7.1 -CDP 850 -- Celltech Aventis Pasteur/Therion Biologics CDP-860 (PEG-PDGF MAb) -- Celltech Cancer vaccine CEA-TRICOM -- Aventis CDP 870 -- Celltech Pasteur/Therion Biologics CDS-1 -- Ernest Orlando Cancer vaccine gene therapy -- Cantab Cedelizumab -- Ortho-McNeil **Pharmaceuticals** Cancer vaccine HER-2/neu - Corixa Cetermin -- Insmed CETP vaccine -- Avant Cancer vaccine THERATOPE -- Biomira Cetrorelix cancer vaccine, PolyMASC - Valentis Cetuximab Candida vaccine - Corixa, Inhibitex CGH 400 -- Novartis Canstatin -- ILEX CGP 42934 - Novartis CAP-18 - Panorama CGP 51901 - Tanox Cardiovascular gene therapy -- Collateral CGRP -- Unigene Therapeutics CGS 27913 - Novartis carperitide -- Suntory CGS 32359 -- Novartis Casocidin-1 -- Pharis CAT 152 - Cambridge Antibody Tech. Chagas disease vaccine -- Corixa chemokines - Immune Response CAT 192 -- Cambridge Antibody Tech. CAT 213 -- Cambridge Antibody Tech. CHH 380 -- Novartis chitinase - Genzyme, ICOS Catalase-- Enzon Chlamydia pneumoniae vaccine -- Antex Cat-PAD -- Circassia CB 0006 -- Celltech Biologics Chlamydia trachomatis vaccine -- Antex CCK(27-32)-- Akzo Nobel CCR2-64I -- NIH Biologics Chlamydia vaccine -- GlaxoSmithKline CD. Procept -- Paligent Cholera vaccine CVD 103-HqR -- Swiss CD154 gene therapy Serum and Vaccine Institute Berne CD39 -- Immunex Cholera vaccine CVD 112 -- Swiss Serum CD39-L2 -- Hvseq CD39-L4 -- Hyseq and Vaccine Institute Berne

FIG. 28H

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Cholera vaccine inactivated oral - SBL CRL 1605 -- CytRx CS-560 -- Sankyo Vaccin CSF -- ZymoGenetics Chrysalin -- Chrysalis BioTech. CSF-G - Hangzhou, Dong-A, Hanmi CI-782 -- Hitachi Kase CSF-GM - Cangene, Hunan, LG Chem Ciliary neurotrophic factor - Fidia, Roche CSF-M -- Zarix CIM project -- Active Biotech CT 1579 - Merck Frosst CL 329753 -- Wyeth-Ayerst CT 1786 - Merck Frosst CL22. Cobra -- ML Laboratories CT-112<sup>^</sup> -- BTG Clenoliximab -- IDEC CTB-134L -- Xenova Clostridium difficile antibodies -- Epicyte CTC-111 -- Kaketsuken clotting factors -- Octagene CTGF -- FibroGen CMB 401 -- Celltech CTLA4-la -- Bristol-Myers Squibb CNTF -- Sigma-Tau CTLA4-lg gene therapy -Cocaine abuse vaccine - Cantab, CTP-37 -- AVI BioPharma ImmuLogic, Scripps C-type natriuretic peptide -- Suntory coccidiomycosis vaccine -- Arizo CVS 995 - Corvas Intl. collagen -- Type I -- Pharming Collagen formation inhibitors -- FibroGen CX 397 – Nikko Kyodo Collagen/hydroxyapatite/bone growth factor CY 1747 -- Epimmune CY 1748 -- Epimmune -- Aventis Pasteur, Biopharm, Orquest Cyanovirin-N collagenase -- BioSpecifics Colorectal cancer vaccine -- Wistar Institute Cystic fibrosis therapy -- CBR/IVAX Component B, Recombinant -- Serono CYT 351 Connective tissue growth factor inhibitors - cytokine Traps - Regeneron cytokines - Enzon, Cytoclonal FibroGen/Taisho Cytomegalovirus glycoprotein vaccine -Contortrostatin Chiron, Aquila Biopharmaceuticals. contraceptive vaccine - Zonagen Aventis Pasteur, Virogenetics Contraceptive vaccine hCG Cytomegalovirus vaccine live -- Aventis Contraceptive vaccine male reversible --Pasteur IMMUCON Cytosine deaminase gene therapy --Contraceptive vaccine zona pellucida --GlaxoSmithKline Zonagen Copper-64 labelled MAb TETA-1A3 - NCI DA-3003 -- Dong-A DAB389interleukin-6 -- Senetek Coralyne DAB389interleukin-7 Corsevin M DAC:GLP-2 -- ConjuChem, Inc. C-peptide analogues -- Schwarz Daclizumab (anti-IL2R MAb) - Protein CPI-1500 -- Consensus Design Labs CRF -- Neurobiological Tech. DAMP<sup>A</sup> -- Incvte Genomics cRGDfV pentapeptide -Daniplestim -- Pharmacia CRL 1095 -- CvtRx darbepoetin alfa - Amgen CRL 1336 -- CvtRx

dural graft matrix -- Integra DBI-3019 -- Diabetogen Duteplase - Baxter Intl. DCC -- Genzyme DWP-401 -- Daewoong DDF -- Hysea DWP-404 -- Daewoong decorin - Integra, Telios DWP-408 -- Daewoong defensins - Large Scale Biology Dx 88 (Epi-KAL2) -- Dyax DEGR-VIIa Dx 890 (elastin inhibitors) -- Dyax Delmmunised antibody 3B6/22 AGEN Deimmunised anti-cancer antibodies -F coli O157 vaccine -- NIH E21-R -- BresaGen Biovation/Viragen Eastern equine encephalitis virus vaccine -Dendroamide A Dengue vaccine -- Bavarian Nordic, Merck Echicetin --Echinhibin 1 denileukin diftitox -- Ligand Echistatin -- Merck DES-1101 -- Desmos Echitamine desirudin -- Novartis Ecromeximab - Kyowa Hakko desmopressin -- Unigene EC-SOD -- PPL Therapeutics Desmoteplase - Merck, Schering AG Eculizumab (5G1.1) -- Alexion Destabilase Diabetes gene therapy - DeveloGen, Pfizer EDF - Ajinomoto FDN derivative -- NIH Diabetes therapy -- Crucell Diabetes type 1 vaccine -- Diamyd FDNA -- NIH Edobacomab -- XOMA Therapeutics DiaCIM -- YM BioSciences Edrecolomab -- Centocor FF 5077 dialytic oligopeptides - Research Corp Ffalizumab -- Genentech Diamyd -- Diamyd Therapeutics EGF fusion toxin - Seragen, Ligand DiaPep227-- Pepgen EGF-P64k vaccine -- Center of Molecular DiavaX -- Corixa Digoxin MAb -- Glaxo Immunology Diphtheria tetanus pertussis-hepatitis B EL 246 -- LigoCyte elastase inhibitor -- Synergen vaccine -- GlaxoSmithKline elcatonin -- Therapicon DIR therapy -- Solis Therapeutics -EMD 72000 - Merck KGaA DNase -- Genentech Dornase alfa -- Genentech Fmdogain -- BIORA emfilermin -- AMRAD Domase alfa, inhalation -- Genentech Doxorubicin-anti-CEA MAb conjugate -Fmoctakin -- Novartis enamel matrix protein -- BIORA Immunomedics DP-107 -- Trimeris Fndo III -- NYU endostatin - EntreMed, Pharis drotrecogin alfa -- Eli Lilly DTctGMCSF Enhancins -- Micrologix Enlimomab -- Isis Pharm. DTP-polio vaccine - Aventis Pasteur Enoxaparin sodium -- Pharmuka DU 257-KM231 antibody conjugate --

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Factor IX gene therapy -- Cell Genesys enzyme linked antibody nutrient depletion Factor VII -- Novo Nordisk, Bayer, Baxter therapy -- KS Biomedix Holdings Eosinophil-derived neutralizing agent -Intl. Factor VIIa -- PPL Therapeutics, EP-51216 -- Asta Medica ZvmoGenetics FP-51389 -- Asta Medica Factor VIII - Bayer Genentech, Beaufour-EPH family ligands -- Regeneron Ipsen, CLB, Inex, Octagen, Pharmacia. Epidermal growth factor -- Hitachi Kasei, Pharming Johnson & Johnson Factor VIII -- PEGylated -- Baver Epidermal growth factor fusion toxin --Factor VIII fragments -- Pharmacia Senetek Factor VIII gene therapy -- Targeted Epidermal growth factor-genistein -Genetics EPI-HNE-4 -- Dyax Factor VIII sucrose formulation - Baver. EPI-KAL2 -- Dyax Epoetin-alfa - Amgen, Dragon Genentech Factor VIII-2 -- Bayer Pharmaceuticals, Nanjing Huaxin Factor VIII-3 -- Bayer Epratuzumab - Immunomedics Factor Xa inhibitors - Merck, Novo Nordisk, Fostein-Barr virus vaccine --Mochida Aviron/SmithKline Beecham, Bioresearch Factor XIII -- ZymoGenetics Eptacog alfa -- Novo Nordisk Factors VIII and IX gene therapy -- Genetics Eptifibatide -- COR Therapeutics Institute/Targeted Genetics erb-38 -Famoxin -- Genset Frlizumab -- Genentech erythropoietin -- Alkermes, ProLease, Dong-Fas (delta) TM protein - LXR BioTech. Fas TR -- Human Genome Sciences A. Elanex, Genetics Institute, LG Chem, Felvizumab -- Scotgen Protein Sciences, Serono, Snow Brand, FFR-VIIa - Novo Nordisk SRC VB VECTOR, Transkaryotic FG-001 - F-Gene Therapies FG-002 - F-Gene Erythropoietin Beta -- Hoffman La Roche Erythropoietin/Epoetin alfa -- Chugai FG-004 - F-Gene Escherichia coli vaccine -- North American FG-005 - F-Gene FGF + fibrin -- Repair Vaccine, SBL Vaccin, Swiss Serum and Fibrimage -- Bio-Tech. General Vaccine Institute Berne fibrin-binding peptides - ISIS Innovation etanercept -- Immunex fibringen -- PPL Therapeutics, Pharming examorelin – Mediolanum fibroblast growth factor - Chiron, NYU. Exendin 4 -- Amylin Ramot, ZymoGenetics exonuclease VII fibrolase conjugate - Schering AG F 105 - Centocor F-992 -- Fornix Filarastim -- Amaen filgrastim -- PDA modified -- Xencor Factor IX -- Alpha Therapeutics, Welfide FLT-3 ligand - Immunex Corp., CSL, enetics Institute/AHP,

Pharmacia, PPL Therapeutics

FN18 CRM9 -

follistatin -- Biotech Australia, Human Therapeutics follitropin alfa - Alkermes, ProLease, PowderJect, Serono, Akzo Nobel Follitropin Beta - Bayer, Organon FP 59 FSH -- Ferring FSH + LH -- Ferring F-spondin -- CeNeS fusion protein delivery system -- UAB Research Foundation fusion toxins - Boston Life Sciences G 5598 -- Genentech GA-II - Transkarvotic Therapies Gamma-interferon analogues -- SRC VB VECTOR Ganirelix -- Roche gastric lipase -- Meristem Gavilimomab -G-CSF - Amgen, SRC VB VECTOR GDF-1 -- CeNeS GDF-5 -- Biopharm GDNF (glial derived neurotrophic factor) -Amaen aelsolin -- Biogen Gemtuzumab ozogamicin - Celltech Gene-activated epoetin-alfa -- Aventis Pharma - Transkaryotic Therapies Glatiramer acetate -- Yeda glial growth factor 2 -- CeNeS GLP-1 - Amylin, Suntory, TheraTech, Watson GLP-1 peptide analogues - Zealand Pharaceuticals GLP-2 - Novo Nordisk, Ontario, Inc., Suntory Limited glucagon -- Eli Lilly, ZymoGenetics Glucagon-like peptide-1 7-36 amide --Suntory Glucogen-like peptide -- Amylin

Glucocerebrosidase -- Genzvme glutamate decarboxylase -- Genzyme Transgenics Glycoprotein S3 -- Kureha GM-CSF -- Immunex GM-CSF tumour vaccine -- PowderJect GnRH immunotherapeutic -- Protherics Goserelin (LhRH antagonist) -- AstraZeneca gp75 antigen - ImClone an96 -- Antigenics GPI 0100 -- Galenica GR 4991W93 -- GlaxoSmithKline Granulocyte colony-stimulating factor --Dong-A Granulocyte colony-stimulating factor conjugate grass allergy therapy -- Dynavax GRF1-44 -- ICN Growth Factor - Chiron, Atrigel, Atrix, Innogenetics, ZymoGenetics, Novo growth factor peptides -- Biotherapeutics growth hormone -- LG Chem growth hormone, Recombinant human --GT 4086 -- Gliatech GW 353430 -- GlaxoSmithKline GW-278884 -- GlaxoSmithKline H 11 -- Viventia Biotech Glanzmann thrombasthenia gene therapy - H5N1 influenza A virus vaccine -- Protein Sciences haemoglobin -- Biopure haemoglobin 3011, Recombinant -- Baxter Healthcare haemoglobin crosfumaril – Baxter Intl. haemoglobin stabilized -- Ajinomoto haemoglobin, recombinant -- Apex HAF -- Immune Response Hantavirus vaccine HB 19 HBNF -- Regeneron

HCC-1 -- Pharis

hCG -- Milkhaus hCG vaccine -- Zonagen HF-317 -- Hollis-Eden Pharmaceuticals Heat shock protein cancer and influenza vaccines - StressGen Helicobacter pylori vaccine - Acambis, AstraZeneca/CSL, Chiron, Provalis Helistat-G - GalaGen Hemolink -- Hemosol hepapoietin -- Snow Brand heparanase -- InSight heparinase I -- Ibex heparinase III -- Ibex Hepatitis A vaccine -- American Biogenetic HIP-- Altachem Sciences Hepatitis A vaccine inactivated Henatitis A vaccine Nothay - Chiron Henatitis A-hepatitis B vaccine --GlaxoSmithKline hepatitis B therapy -- Tripep Henatitis B vaccine - Amgen, Chiron SpA, Meiji Milk, NIS, Prodeva, PowderJect, Rhein Biotech Henatitis B vaccine recombinant -- Evans Vaccines, Epitec Combiotech, Genentech, Medlmmune, Merck Sharp & Dohme, Rhein Biotech, Shantha Biotechnics, Vector, Yeda Hepatitis B vaccine recombinant TGP 943 - HIV immune globulin - Abbott, Chiron Takeda Hepatitis C vaccine -- Bavarian Nordic. Chiron, Innogenetics Acambis, Hepatitis D vaccine -- Chiron Vaccines Henatitis E vaccine recombinant --

Sosei hepatocyte growth factor kringle fragments -- EntreMed

Genelabs/GlaxoSmithKline, Novavax hepatocyte growth factor - Panorama,

Her-2/Neu peptides -- Corixa

Herpes simplex glycoprotein DNA vaccine -Merck, Wyeth-Lederle Vaccines-Malvern, Genentech, GlaxoSmithKline, Chiron, Takeda

Herpes simplex vaccine -- Cantab Pharmaceuticals, CEL-SCI, Henderson Morley

Herpes simplex vaccine live -- ImClone Systems/Wyeth-Lederle, Aventis Pasteur HGF derivatives - Dompe hIAPP vaccine -- Crucell Hib-hepatitis B vaccine -- Aventis Pasteur

HIC 1 Hirudins - Biopharma, Cangene, Dongkook, Japan Energy Corporation, Pharmacia Corporation, SIR International, Sanofi-Synthelabo, Sotragene, Rhein Biotech HIV edible vaccine -- ProdiGene HIV ap120 vaccine - Chiron, Ailnomoto, GlaxoSmithKline, ID Vaccine, Progenics, VaxGen HIV gp120 vaccine gene therapy -HIV ap160 DNA vaccine - PowderJect. Aventis Pasteur, Oncogen, Hyland Immuno. Protein Sciences HIV gp41 vaccine -- Panacos HIV HGP-30W vaccine -- CEL-SCI

HIV peptides -- American Home Products HIV vaccine -- Applied bioTech., Axis Genetics, Biogen, Bristol-Myers Squibb, Genentech, Korea Green Cross, NIS, Oncogen, Protein Sciences Corporation, Terumo, Tonen Corporation, Wyeth-Averst, Wyeth-Lederle Vaccines-Malvern, Advanced BioScience Laboratories. Bavarian Nordic, Bavarian Nordic/Statens

Serum Institute, GeneCure, Immune Response, Progenics, Therion Biologics, United Biomedical. Chiron

### FIG. 28M

HIV vaccine vCP1433 -- Aventis Pasteur HIV vaccine vCP1452 -- Aventis Pasteur HIV vaccine vCP205 -- Aventis Pasteur HL-9 -- American BioScience HM-9239 - Cytran HML-103 -- Hemosol HML-104 -- Hemosol HMI -105 -- Hemosol HMI -109 -- Hemosol HMI -110 -- Hemosol HMI -121 -- Hemosol hNLP -- Pharis Hookworm vaccine host-vector vaccines -- Henogen HPM 1 -- Chugai HPV vaccine -- MediGene HSA -- Meristem HSF -- StressGen HSP carriers -Weizmann, Yeda, Peptor HSPPC-70 -- Antigenics HSV 863 -- Novartis HTI V-I DNA vaccine HTLV-I vaccine HTI V-II vaccine -- Access HU 901 - Tanox Hu23F2G -- ICOS HuHMFG1 Humal YM -- Intracell Human krebs statika -- Yamanouchi human monoclonal antibodies --Abgenix/Biogen, Abgenix/ Corixa, Abgenix/Immunex, Abgenix/Lexicon, Abgenix/ Pfizer, Athersys/Medarex, Biogen/MorphoSys, CAT/Searle. Centocor/Medarex, Corixa/Kirin Brewery, Corixa/Medarex, Eos BioTech./Medarex, Fos/Xenerex, Exelixis/Protein Design Labs, ImmunoGen/ Raven, Medarex/ B.Twelve, MorphoSys/ImmunoGen, XTL Biopharmaceuticals/Dyax,

Human monoclonal antibodies --Medarex/Northwest Biotherapeutics. Medarex/Seattle Genetics human netrin-1 -- Exelixis human papillomavirus antibodies - Epicyte Human papillomavirus vaccine - Biotech Australia, IDEC, StressGen Human papillomavirus vaccine MEDI 501 --MedImmune/GlaxoSmithKline Human papillomavirus vaccine MEDI 503/MEDI 504 --MedImmune/GlaxoSmithKline Human papillomavirus vaccine TA-CIN -Cantab Pharmaceuticals Human papillomavirus vaccine TA-HPV --Cantab Pharmaceuticals Human papillomavirus vaccine TH-GW --Cantab/GlaxoSmithKline human polyclonal antibodies -- Biosite/Eos BioTech./ Medarex HSPPC-96, pathogen-derived -- Antigenics human type II anti factor VIII monoclonal antibodies -- ThromboGenics humanised anti glycoprotein Ib murine monoclonal antibodies -- ThromboGenics HumaRAD -- Intracell HuMax EGFR -- Genmab HuMax-CD4 -- Medarex HuMax-IL15 -- Genmab HYB 190 -- Hybridon HYB 676 -- Hybridon I-125 MAb A33 -- Celltech Ibritumomab tiuxetan -- IDEC IBT-9401 -- Ibex IBT-9402 -- Ibex IC 14 -- ICOS Idarubicin anti-Ly-2.1 -IDEC 114 -- IDEC IDEC 131 -- IDEC IDEC 152 -- IDEC IDM 1 -- IDM IDPS -- Hollis-Eden Pharmaceuticals

iduronate-2-sulfatase -- Transkaryotic Therapies IGF/IBP-2-13 - Pharis IGN-101 -- laeneon IK HIR02 – Iketon IL-11 -- Genetics Institute/AHP IL-13-PE38 -- NeoPharm IL-17 receptor -- Immunex IL-18BP -- Yeda IL-1Hv1 -- Hvseq IL-1ß -- Celltech IL-1ß adjuvant -- Celltech IL-2 -- Chiron IL-2 + IL-12 -- Hoffman La-Roche IL-6/sIL-6R fusion - Hadasit IL-6R derivative - Tosoh IL-7-Dap 389 fusion toxin - Ligand IL-21 - Novo Nordisk, ZymoGenetics IM-862 -- Cytran IMC-1C11 -- ImClone imiglucerase -- Genzyme Immune globulin intravenous (human) --Hoffman La Roche immune privilege factor -- Proneuron Immunocal -- Immunotec Immunogene therapy - Briana Bio-Tech Immunoliposomal 5-fluorodeoxyuridinedipalmitate immunosuppressant vaccine -- Aixlie immunotoxin - Antisoma, NIH ImmuRAIT-Re-188 - Immunomedics imreg-1 - Imreg infertility - Johnson & Johnson, E-TRANS Infliximab -- Centocor Influenza virus vaccine -- Aventis Pasteur. Protein Sciences inhibin -- Biotech Australia, Human Therapeutics Inhibitory G protein gene therapy INKP-2001 -- InKine Inclimomab -- Diaclone

insulin -- AutoImmune, Altea, Biobras, BioSante, Bio-Tech. General, Chong Kun Dang, Emisphere, Flamel, Provalis, Rhein Biotech, TranXenoGen insulin (bovine) -- Novartis insulin analogue -- Eli Lilly Insulin Aspart -- Novo Nordisk insulin detemir - Novo Nordisk insulin alargine -- Aventis insulin inhaled - Inhale Therapeutics Systems, Alkermes insulin oral -- Inovax insulin, AeroDose -- AeroGen insulin, AERx -- Aradigm insulin, BEODAS -- Elan insulin, Biphasix -- Helix insulin, buccal -- Generex insulin, I2R - Flemington insulin, intranasal -- Bentley insulin, oral - Nobex, Unigene insulin. Orasome -- Endorex insulin, ProMaxx -- Epic insulin, Quadrant -- Elan insulin, recombinant -- Aventis insulin. Spiros -- Elan insulin. Transfersome -- IDEA insulin, Zvmo, recombinant - Novo Nordisk insulinotropin -- Scios Insulvsin gene therapy integrin antagonists -- Merck interferon (Alpha2) -- SRC VB VECTOR, Viragen, Dong-A, Hoffman La-Roche. Genentech interferon - BioMedicines, Human Genome Sciences interferon (Alfa-n3)-Interferon Sciences interferon (Alpha), Biphasix -- Helix

interferon (Alpha)-Amgen, BioNative, Novartis, Genzyme Transgenics, Havashibara, Inhale Therapeutics Systems, Medusa, Flamel, Dong-A, GeneTrol, Nastech, Shantha, Wassermann, LG Chem, Sumitomo, Aventis, Behring EGIS, Pepgen, Servier, Rhein Biotech, interferon (Alpha2A) interferon (Alpha2B) - Enzon, Schering-Plough, Biogen, IDEA interferon (Alpha-N1) -- GlaxoSmithKline interferon (beta) - Rentschler, GeneTrol, Meristem, Rhein Biotech, Toray, Yeda, Dajichi, Mochida interferon (Beta1A) - Serono, Biogen interferon (beta1A), inhale - Biogen interferon (ß1b)-- Chiron interferon (tau) -- Pepgen Interferon alfacon-1 -- Amgen Interferon alpha-2a vaccine Interferon Beta 1b -- Schering/Chiron, InterMune Interferon Gamma -- Boehringer Ingelheim, Sheffield, Rentschler, Hayashibara interferon receptor, Type I -- Serono interferon(Gamma1B) -- Genentech Interferon-alpha-2b + ribavirin - Biogen, ICN Interferon-alpha-2b gene therapy --Schering-Plough Interferon-con1 gene therapy interleukin-1 antagonists - Dompe Interleukin-1 receptor antagonist - Abbott Bioresearch, Pharmacia Interleukin-1 receptor type I -- Immunex interleukin-1 receptor Type II -- Immunex Interleukin-1 trap -- Regeneron Interleukin-1-alpha -- Immunex/Roche interleukin-2 -- SRC VB VECTOR. Aiinomoto, Biomira, Chiron

IL-2/ diphtheria toxin -- Ligand Interleukin-3 -- Cangene Interleukin-4 -- Immunology Ventures, Sanofi Winthrop, Schering-Plough, Immunex/ Sanofi Winthrop, Bayer, Ono interleukin-4 + TNF-Alpha -- NIH interleukin-4 agonist - Bayer interleukin-4 fusion toxin -- Ligand Interleukin-4 receptor - Immunex, Immun Interleukin-6 - Ajinomoto, Cangene, Yeda, Genetics Institute, Novartis interleukin-6 fusion protein interleukin-6 fusion toxin - Ligand, Serono interleukin-7 -- IC Innovations interleukin-7 receptor -- Immunex interleukin-8 antagonists -- Kyowa Hakko/Millennium/Pfizer interleukin-9 antagonists -- Genaera Interleukin-10 - DNAX, Schering-Plough Interleukin-10 gene therapy interleukin-12 -- Genetics Institute, Hoffman La-Roche interleukin-13 - Sanofi interleukin-13 antagonists -- AMRAD Interleukin-13-PE38QQR interleukin-15 -- Immunex interleukin-16 -- Research Corp interleukin-18 -- GlaxoSmithKline Interleukin-18 binding protein -- Serono lor-P3 -- Center of Molecular Immunology IP-10 -- NIH IPF -- Metabolex IR-501 -- Immune Response ISIS 9125 -- Isis Pharmaceuticals ISURF No. 1554 -- Millennium ISURF No. 1866 - Iowa State Univer. ITF-1697 -- Italfarmaco IxC 162 - Ixion J 695 - Cambridge Antibody Tech., Genetics Inst., Knoll

Jagged + FGF -- Repair

JKC-362 Phoenix Pharmaceuticals	leptin, 2nd-generation Amgen
JTP-2942 - Japan Tobacce	leridistim Pharmacia
Juman monoclonal antibodies	leuprolide, ProMaxx Epic
Medarex/Raven	leuprorelin, oral Unigene
K02 Axys Pharmaceuticals	LeuTech - Papatin
Keliximab IDEC	LEX 032 SuperGen
Keyhole limpet haemocyanin	LIDEPT Novartis
KGF Amgen	Lintuzumab (anti-CD33 MAb) Protein
KM 871 Kyowa	Design Labs
KPI 135 Scios	lipase Altus Biologics
KPI-022 Scios	lipid A vaccine - EntreMed
Kringle 5	lipid-linked anchor Tech ICRT, ID
KSB 304	Biomedical
KSB-201 KS Biomedix	liposome-CD4 Tech Sheffield
L 696418 Merck	Listeria monocytogenes vaccine
L 703801 Merck	LMB 1
L1 Acorda	LMB 7
L-761191 - Merck	LMB 9 Battelle Memorial Institute, NIH
lactoferrin - Meristem, Pharming, Agennix	LM-CD45 Cantab Pharmaceuticals
lactoferrin cardio Pharming	Iovastatin Merck
LAG-3 Serono	LSA-3
LAIT GEMMA	LT-ß receptor Biogen
LAK cell cytotoxin Arizona	lung cancer vaccine Corixa
lamellarins PharmaMar/University of	lusupultide Scios
Malaga	L-Vax AVAX
laminin A peptides NIH	LY 355455 Eli Lilly
lanoteplase Genetics Institute	LY 366405 Eli Lilly
laronidase BioMarin	LY-355101 Eli Lilly
Lassa fever vaccine	Lyme disease DNA vaccine Vical/Aventis
LCAT NIH	Pasteur
LDP 01 Millennium	Lyme disease vaccine Aquila
LDP 02 - Millennium	Biopharmaceuticals, Aventis, Pasteur,
Lecithinized superoxide dismutase -	Symbicom, GlaxoSmithKline, Hyland
Seikagaku	Immuno, MedImmune
LeIF adjuvant Corixa	Lymphocytic choriomeningitis virus vaccine
leishmaniasis vaccine Corixa	lymphoma vaccine – Biomira, Genitope
lenercept Hoffman La-Roche	LYP18
Lenograstim - Aventis, Chugai	lys plasminogen, recombinant
lepirudin Aventis	Lysosomal storage disease gene therapy -
leptin - Amgen, IC Innovations	Avigen
Leptin gene therapy Chiron Corporation	lysostaphin Nutrition 21

M 23 -- Gruenenthal M1 monoclonal antibodies -- Acorda Therapeutics MA 16N7C2 - Corvas Intl. malaria vaccine -- GlaxoSmithKline. AdProTech, Antigenics, Apovia, Aventis Pasteur, Axis Genetics, Behringwerke, CDCP, Chiron Vaccines, Genzyme Transgenics, Hawaii, MedImmune, NIH, NYU. Oxxon, Roche/Saramane, Biotech Australia, Rx Tech Malaria vaccine CDC/NIIMALVAC-1 malaria vaccine.multicomponent mammaglobin -- Corixa mammastatin -- Biotherapeutics mannan-binding lectin -- Natlmmu mannan-MUC1 -- Psiron MAP 30 Marinovir -- Phytera MARstem -- Maret MB-015 -- Mochida MBP -- ImmuLogic MCI-028 -- Mitsubishi-Tokyo MCIF -- Human Genome Sciences MDC -- Advanced BioScience -- Akzo Nobel, ICOS MDX 11 -- Medarex MDX 210 -- Medarex MDX 22 -- Medarex MDX 22 MDX 240 - Medarex MDX 33 MDX 44 -- Medarex MDX 447 -- Medarex MDX H210 -- Medarex MDX RA -- Houston BioTech., Medarex ME-104 -- Pharmexa Measles vaccine Mecasermin -- Cephalon/Chiron, Chiron MEDI 488 -- Medimmune MEDI 500

MEDI 507 -- BioTransplant melanin concentrating hormone --Neurocrine Biosciences melanocortins -- OMRF Melanoma monoclonal antibodies -- Viragen melanoma vaccine - GlaxoSmithKline, Akzo Nobel, Avant, Aventis Pasteur, Bavarian Nordic, Biovector, CancerVax, Genzyme Molecular Oncology, Humbolt, ImClone Systems, Memorial, NYU, Oxxon Melanoma vaccine Magevac -- Therion memory enhancers -- Scios meningococcal B vaccine -- Chiron meningococcal vaccine -- CAMR Meningococcal vaccine group B conjugate - North American Vaccine Meningococcal vaccine group B recombinant -- BioChem Vaccines. Microscience Meningococcal vaccine group Y conjugate -- North American Vaccine Meningococcal vaccine groups A B and C conjugate -- North American Vaccine Mepolizumab - GlaxoSmithKline Metastatin - EntreMed, Takeda Met-CkB7 -- Human Genome Sciences met-enkephalin -- TNI METH-1 -- Human Genome Sciences methioninase -- AntiCancer Methionine lyase gene therapy --AntiCancer Met-RANTES - Genexa Biomedical. Serono Metreleptin Microtubule inhibitor MAb Immunogen/Abgenix MGDF -- Kirin MGV -- Progenics micrin -- Endocrine microplasmin -- ThromboGenics

MIF -- Genetics Institute

MAb 45-2D9- - haematoporphyrin migration inhibitory factor - NIH conjugate Mim CD4.1 – Xycte Therapies mirostipen -- Human Genome Sciences MAb 4B4 Mitumomab (BEC-2) - ImClone Systems. MAb 4E3-CPA conjugate -- BCM Oncologia MAh 4E3-daunorubicin conjugate Merck KGaA MAb 50-6 MK 852 -- Merck MAb 50-61A - Institut Pasteur MLN 1202 (Anti-CCR2 monoclonal antibody) - Millenium Pharmaceuticals MAb 5A8 - Biogen MAb 791T/36-methotrexate conjugate Mohenakin -- NIS molgramostim -- Genetics Institute, Novartis MAb 7c11.e8 monoclonal antibodies -- Abgenix/Celltech, MAb 7E11 C5-selenocystamine conjugate MAb 93KA9 -- Novartis Immusol/ Medarex, Viragen/ Roslin Institute, Cambridge Antibody Tech./Elan MAb A5B7-cisplatin conjugate --Biodynamics Research, Pharmacia MAb 108 -MAb A5B7-I-131 MAb 10D5 --MAb 14.18-interleukin-2 immunocytokine -- MAb A7 MAh A717 -- Exocell Lexiden MAb A7-zinostatin conjugate MAb 14G2a -MAb ABX-RB2 - Abgenix MAh 15A10 -MAh ACA 11 MAb 170 -- Biomira MAb AFP-I-131 - Immunomedics MAb 177Lu CC49 --MAb AP1 MAb 17F9 MAb AZ1 MAb 1D7 MAb B3-LysPE40 conjugate MAb 1F7 - Immune Network MAb B4 - United Biomedical MAb 1H10-doxorubicin conjugate MAb B43 Genistein-conjugate MAb 26-2F MAb B43.13-Tc-99m -- Biomira MAb 2A11 MAb B43-PAP conjugate MAb 2E1 -- RW Johnson MAb B4G7-gelonin conjugate MAb 2F5 MAb BCM 43-daunorubicin conjugate --MAb 31.1 -- International Biolmmune BCM Oncologia Systems MAb 32 -- Cambridge Antibody Tech., MAb BIS-1 MAb BMS 181170 -- Bristol-Myers Squibb Pentech MAb 323A3 -- Centocor MAb BR55-2 MAb BW494 MAb 3C5 MAb C 242-DM1 conjugate -- ImmunoGen MAb 3F12 MAb C242-PE conjugate MAb 3F8 MAb c30-6 MAh 42/6 MAb CA208-cytorhodin-S conjugate --MAb 425 - Merck KGaA Hoechst Japan MAb 447-52D -- Merck Sharp & Dohme MAb CC49 -- Enzon

#### WO 2004/033651

MAh LiCO 16-88

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MAb LL2-I-131 - Immunomedics MAb ch14.18 -MAb LL2-Y-90 MAb CH14.18-GM-CSF fusion protein --MAb LS2D617 -- Hybritech Lexiaen MAb LYM-1-gelonin conjugate MAb chCE7 MAb LYM-1-I-131 MAb CI-137 -- AMRAD MAb LYM-1-Y-90 MAb cisplatin conjugate MAb LYM-2 -- Peregrine MAb CLB-CD19 MAb M195 MAb CLB-CD19v MAb M195-bismuth 213 conjugate --MAb CLL-1 -- Peregrine Protein Design Labs MAb CLL-1-GM-CSF conjugate MAb CLL-1-IL-2 conjugate -- Peregrine MAb M195-gelonin conjugate MAb CLN IgG -- doxorubicin conjugates MAb M195-I-131 MAb M195-Y-90 MAb conjugates - Tanox MAb MA 33H1 - Sanofi MAb D612 MAb MAD11 MAb Dal B02 MAb MGb2 MAb DC101 -- ImClone MAb MINT5 MAb EA 1 -MAb MK2-23 MAb EC708 -- Biovation MAb MOC31 ETA(252-613) conjugate MAb EP-5C7 -- Protein Design Labs MAh MOC-31-In-111 MAb ERIC-1 -- ICRT MAb MOC-31-PE conjugate MAb F105 gene therapy MAb MR6 -MAb FC 2.15 MAh MRK-16 -- Aventis Pasteur MAb G250 -- Centocor MAh MS11G6 MAb GA6 MAb MX-DTPA BrE-3 MAh GA733 MAb MY9 MAh Gliomah-H -- Viventia Biotech MAb Nd2 -- Tosoh MAb HB2-saporin conjugate MAb NG-1 -- Hygeia MAb HD 37 -MAb NM01 - Nissin Food MAh HD37-ricin chain-A conjugate MAh HNK20 -- Acambis MAb OC 125 MAb OC 125-CMA conjugate MAb huN901-DM1 conjugate --MAb OKI-1 -- Ortho-McNeil ImmunoGen MAb OX52 -- Bioproducts for Science MAb I-131 CC49 -- Corixa MAb PMA5 MAb ICO25 MAb ICR12-CPG2 conjugate MAb PR1 MAb prost 30 MAb ICR-62 MAb IRac-ricin A conjugate MAh R-24 MAb R-24 α Human GD3 - Celltech MAh K1 MAb RFB4-ricin chain A conjugate MAb KS1-4-methotrexate conjugate MAb RFT5-ricin chain A conjugate MAb L6 -- Bristol-Myers Squibb, Oncogen MAb SC 1

MAb SM-3 ICRT	Muc-1 vaccine Corixa
MAb SMART 1D10 Protein Design Labs	mucosal tolerance Aberdeen
MAb SMART ABL 364 Novartis	mullerian inhibiting subst
MAb SN6f	muplestim - Genetics Institute, Novartis,
MAb SN6f-deglycosylated ricin A chain	DSM Anti-Infectives
conjugate -	murine MAb KS Biomedix
MAb SN6j	Mutant somatropin JCR Pharmaceutical
MAb SN7-ricin chain A conjugate	MV 833 Toagosei
MAb T101-Y-90 conjugate Hybritech	Mycoplasma pulmonis vaccine
MAb T-88 Chiron	Mycoprex XOMA
MAb TB94 Cancer ImmunoBiology	myeloperoxidase Henogen
MAb TEC 11	myostatin Genetics Institute
MAb TES-23 Chugai	Nacolomab tafenatox Pharmacia
MAb TM31 Avant	Nagrecor Scios
MAb TNT-1 Cambridge Antibody Tech.,	nagrestipen British Biotech
Peregrine	NAP-5 – Corvas Intl.
MAb TNT-3	NAPc2 – Corvas Intl.
MAb TNT-3 IL2 fusion protein -	nartograstim Kyowa
MAb TP3-At-211	Natalizumab Protein Design Labs
MAb TP3-PAP conjugate –	Nateplase – NIH, Nihon Schering
MAb UJ13A ICRT	nateplase Schering AG
MAb UN3	NBI-3001 Neurocrine Biosci.
MAb ZME-018-gelonin conjugate	NBI-5788 Neurocrine Biosci.
MAb-BC2 GlaxoSmithKline	NBI-6024 Neurocrine Biosci.
MAb-DM1 conjugate ImmunoGen	Nef inhibitors BRI
MAb-ricin-chain-A conjugate XOMA	Neisseria gonorrhoea vaccine Antex
MAb-temoporfin conjugates	Biologics
Monopharm C Viventia Biotech	Neomycin B-arginine conjugate
monteplase Eisai	Nerelimomab Chiron
montirelin hydrate Gruenenthal	Nerve growth factor – Amgen – Chiron,
moroctocog alfa Genetics Institute	Genentech
Moroctocog-alfa Pharmacia	Nerve growth factor gene therapy
MP 4	nesiritide citrate Scios
MP-121 Biopharm	neuregulin-2 CeNeS
MP-52 Biopharm	neurocan NYU
MRA Chugai	neuronal delivery system CAMR
MS 28168 Mitsui Chemicals, Nihon	Neurophil inhibitory Factor Corvas
Schering	Neuroprotective vaccine University of
MSH fusion toxin Ligand	Auckland
MSI-99 Genaera	neurotrophic chimaeras Regeneron
MT 201 Micromet	neurotrophic factor - NsGene, CereMedix

NeuroVax -- Immune Response neurturin -- Genentech neutral endopeptidase -- Genentech NGF enhancers -- NeuroSearch NHL vaccine -- Large Scale Biology NIP45 -- Boston Life Sciences NKI-B20 NM 01 - Nissin Food NMI-139 -- NitroMed NMMP -- Genetics Institute NN-2211 -- Novo Nordisk Noggin -- Regeneron Nonacog alfa Norelin -- Biostar Norwalk virus vaccine NRLU 10 -- NeoRx NRLU 10 PE -- NeoRx NT-3 -- Regeneron NT-4/5 -- Genentech NU 3056 NU 3076 NX 1838 -- Gilead Sciences NY ESO-1/CAG-3 antigen -- NIH NYVAC-7 -- Aventis Pasteur NZ-1002 -- Novazyme obesity therapy -- Nobex OC 10426 -- Ontogen OC 144093 -- Ontogen OCIF -- Sankvo Oct-43 -- Otsuka Odulimomab -- Immunotech OK PSA - liposomal OKT3-gamma-1-ala-ala OM 991 OM 992 Omalizumab -- Genentech oncoimmunin-L -- NIH Oncolysin B -- ImmunoGen Oncolvsin CD6 -- ImmunoGen Oncolysin M -- ImmunoGen Oncolysin S -- ImmunoGen

Oncophage -- Antigenics Oncostatin M -- Bristol-Myers Squibb OncoVax-CL -- Jenner Biotherapies OncoVax-P -- Jenner Biotherapies onercept -- Yeda onychomycosis vaccine -- Boehringer Ingelheim opebecan -- XOMA opioids -- Arizona Oprelvekin - Genetics Institute Oregovomab -- AltaRex Org-33408 b-- Akzo Nobel Orolip DP -- EpiCept orvzacystatin OSA peptides - GenSci Regeneration osteoblast-cadherin GF -- Pharis Osteocalcin-thymidine kinase gene therapy osteogenic protein -- Curis osteopontin -- OraPharma osteoporosis peptides - Integra, Telios osteoprotegerin - Amgen, SnowBrand otitis media vaccines -- Antex Biologics ovarian cancer - University of Alabama OX40-IgG fusion protein -- Cantab, Xenova P 246 -- Diatide P 30 -- Alfacell p1025 -- Active Biotech P-113<sup>^</sup> -- Demegen P-16 peptide -- Transition Therapeutics p43 -- Ramot P-50 peptide -- Transition Therapeutics p53 + RAS vaccine -- NIH, NCI PACAP(1-27) analogue paediatric vaccines -- Chiron Pafase -- ICOS PAGE-4 plasmid DNA -- IDEC PAI-2 - Biotech Australia. Human Therapeutics Palifermin (keratinocyte growth factor) --Amaen Palivizumab -- Medimmune

### **FIG. 28V**

PAM 4 -- Merck namiteplase -- Yamanouchi pancreatin, Minitabs -- Eurand Pangen -- Fournier Pantarin - Selective Genetics Parainfluenza virus vaccine - Pharmacia, Pierre Fahre paraoxanase -- Esperion parathyroid hormone - Abiogen, Korea Green Cross Parathyroid hormone (1-34) --Chugai/Suntory Parkinson's disease gene therapy -- Cell Genesys/ Ceregene Parvovirus vaccine -- MedImmune PCP-Scan - Immunomedics PDGF -- Chiron PDGF cocktail -- Theratechnologies peanut allergy therapy - Dynavax PEG anti-ICAM MAb - Boehringer Ingelheim PEG asparaginase -- Enzon PEG alucocerebrosidase PEG hirudin - Knoll PEG interferon-alpha-2a -- Roche PEG interferon-alpha-2b + ribavirin -Biogen, Enzon, ICN Pharmaceuticals, Schering-Plough PEG MAb A5B7 -Pegacaristim - Amgen -- Kirin Brewery --ZvmoGenetics Pegaldesleukin -- Research Corp pegaspargase -- Enzon pegfilgrastim -- Amgen PEG-interferon Alpha -- Viragen PEG-interferon Alpha 2A -- Hoffman La-Roche PEG-interferon Alpha 2B -- Schering-Plough PEG-r-hirudin -- Abbott PEG-rHuMGDF -- Amgen

PEG-uricase -- Mountain View Pegvisomant - Genentech PEGylated proteins, PolyMASC -- Valentis PEGylated recombinant native human leptin -- Roche Pemtumomab Penetratin -- Cyclacel Pepscan - Antisoma peptide G - Peptech, ICRT peptide vaccine - NIH ,NCI Pexelizumab pexiganan acetate -- Genaera Pharmaprojects No. 3179 -- NYU Pharmaprojects No. 3390 -- Ernest Orlando Pharmaprojects No. 3417 -- Sumitomo Pharmaprojects No. 3777 -- Acambis Pharmaprojects No. 4209 -- XOMA Pharmaprojects No. 4349 - Baxter Intl. Pharmaprojects No. 4651 Pharmaprojects No. 4915 -- Avanir Pharmaprojects No. 5156 -- Rhizogenics Pharmaprojects No. 5200 -- Pfizer Pharmaprojects No. 5215 -- Origene Pharmaprojects No. 5216 -- Origene Pharmaprojects No. 5218 -- Origene Pharmaprojects No. 5267 - ML Laboratories Pharmaprojects No. 5373 -- MorphoSvs Pharmaprojects No. 5493 -- Metabolex Pharmaprojects No. 5707 -- Genentech Pharmaprojects No. 5728 -- Autogen Pharmaprojects No. 5733 -- BioMarin Pharmaprojects No. 5757 -- NIH Pharmaprojects No. 5765 -- Gryphon Pharmaprojects No. 5830 -- AntiCancer Pharmaprojects No. 5839 -- Dyax Pharmaprojects No. 5849 -- Johnson & Johnson Pharmaprojects No. 5860 -- Mitsubishi-

Tokvo

Pharmaprojects No. 5869 - Oxford **GlycoSciences** Pharmaprojects No. 5883 -- Asahi Brewery Pharmaprojects No. 5947 -- StressGen Pharmaprojects No. 5961 --Theratechnologies Pharmaprojects No. 5962 -- NIH Pharmaprojects No. 5966 -- NIH Pharmaprojects No. 5994 -- Pharming Pharmaprojects No. 5995 - Pharming Pharmaprojects No. 6023 -- IMMUCON Pharmaprojects No. 6063 -- Cytoclonal Pharmaprojects No. 6073 -- SIDDCO Pharmaprojects No. 6115 -- Genzyme Pharmaprojects No. 6227 -- NIH Pharmaprojects No. 6230 -- NIH Pharmaprojects No. 6236 -- NIH Pharmaprojects No. 6243 -- NIH Pharmaprojects No. 6244 -- NIH Pharmaprojects No. 6281 -- Senetek Pharmaprojects No. 6365 -- NIH Pharmaprojects No. 6368 -- NIH Pharmaprojects No. 6373 -- NIH Pharmaprojects No. 6408 - Pan Pacific Pharmaprojects No. 6410 - Athersys Pharmaprojects No. 6421 - Oxford GlycoSciences Pharmaprojects No. 6522 -- Maxvoen Pharmaprojects No. 6523 -- Pharis Pharmaprojects No. 6538 -- Maxygen Pharmaprojects No. 6554 -- APALEXO Pharmaprojects No. 6560 -- Ardana Pharmaprojects No. 6562 -- Baver Pharmaprojects No. 6569 -- Eos Phenoxazine Phenylase -- Ibex Pigment epithelium derived factor plasminogen activator inhibitor-1, recombinant -- DuPont Pharmaceuticals

Plasminogen activators - Abbott Laboratories, American Home Products, Boehringer Mannheim, Chiron Corporation, DuPont Pharmaceuticals, Eli Lilly, Shionogi, Genentech, Genetics Institute, GlaxoSmithKline, Hemispherx Biopharma, Merck & Co, Novartis, Pharmacia Corporation, Wakamoto, Yeda plasminogen-related peptides -- Bio-Tech. General/MGH platelet factor 4 -- RepliGen Platelet-derived growth factor - Amgen --ZvmoGenetics plusonermin- Havashibara PMD-2850 -- Protherics Pneumococcal vaccine -- Antex Biologics, Aventis Pasteur Pneumococcal vaccine intranasal --BioChem Vaccines/Biovector PR1A3 PR-39 pralmorelin -- Kaken Pretarget-Lymphoma -- NeoRx Priliximab -- Centocor PRO 140 -- Progenics PRO 2000 -- Procept PRO 367 -- Progenics PRO 542 -- Progenics pro-Apo A-I -- Esperion prolactin -- Genzyme Prosaptide TX14(A) -- Bio-Tech. General prostate cancer antbodies - Immunex, UroCor prostate cancer antibody therapy --Genentech/UroGenesys, Genotherapeutics prostate cancer immunotherapeutics -- The PSMA Development Company prostate cancer vaccine -- Aventis Pasteur,

Zonagen, Corixa, Dendreon, Jenner Biotherapies, Therion Biologics

prostate-specific antigen -- EntreMed RD 62198 rDnase -- Genentech protein A -- RepliGen RDP-58 -- SangStat protein adhesives -- Enzon RecepTox-Fce -- Kervx protein C - Baxter Intl., PPL Therapeutics, RecepTox-GnRH - Keryx, MTR ZvmoGenetics protein C activator - Gilead Sciences Technologies RecepTox-MBP - Keryx, MTR protein kinase R antags -- NIH Technologies protirelin -- Takeda recFSH -- Akzo Nobel, Organon protocadherin 2 -- Caprion Pro-urokinase - Abbott, Bristol-Myers REGA 3G12 Regavirumab -- Teijin Squibb, Dainippon, Tosoh -- Welfide P-selectin glycoprotein ligand-1 -- Genetics relaxin -- Connetics Corp Renal cancer vaccine -- Macropharm Institute repifermin -- Human Genome Sciences pseudomonal infections -- InterMune Respiratory syncytial virus PFP-2 vaccine --Pseudomonas vaccine -- Cytovax Wveth-Lederle PSGL-Ig -- American Home Products Respiratory syncytial virus vaccine -PSP-94 - Procvon GlaxoSmithKline, Pharmacia, Pierre Fabre PTH 1-34 -- Nobex Respiratory syncytial virus vaccine Quilimmune-M -- Antigenics inactivated R 744 - Roche Respiratory syncytial virus-parainfluenza R 101933 virus vaccine -- Aventis Pasteur, R 125224 -- Sankvo Pharmacia RA therapy -- Cardion Rabies vaccine recombinant -- Aventis Reteplase -- Boehringer Mannheim, Hoffman La-Roche Pasteur, BioChem Vaccines, Kaketsuken Retropep -- Retroscreen Pharmaceuticals 3 4 1 RFB4 (dsFv) PE38 RadioTheraCIM -- YM BioSciences RFI 641 -- American Home Products Ramot project No. 1315 -- Ramot RFTS -- UAB Research Foundation Ramot project No. K-734A -- Ramot RG 12986 -- Aventis Pasteur Ramot project No. K-734B -- Ramot RG 83852 -- Aventis Pasteur Ranibizumab (Anti-VEGF fragment) --RG-1059 -- RepliGen Genentech rGCR -- NIH RANK -- Immunex rGLP-1 -- Restoragen rannirnase -- Alfacell ranpirnase-anti-CD22 MAb -- Alfacell rGRF -- Restoragen rh Insulin - Eli Lilly RANTES inhibitor -- Milan RHAMM targeting peptides - Cangene RAPID drug delivery systems -- ARIAD rHb1.1 - Baxter Intl. rasburicase -- Sanofi rhCC10 -- Claragen rBPI-21, topical -- XOMA rhCG -- Serono RC 529 -- Corixa Rheumatoid arthritis gene therapy rCFTR -- Genzyme Transgenics

SB RA 31012 -Rheumatoid arthritis vaccine -- Veterans SC 56929 -- Pharmacia Affairs Medical Center SCA binding proteins - Curis, Enzon rhl H -- Serono scFv(14E1)-ETA Berlex Laboratories. Ribozyme gene therapy -- Genset Schering AG Rickettsial vaccine recombinant ScFv(FRP5)-ETA -RIGScan CR - Neoprobe ScFv6C6-PE40 -RIP-3 -- Rigel SCH 55700 - Celltech Rituximab -- Genentech Schistosomiasis vaccine -- Glaxo RK-0202 -- RxKinetix Wellcome/Medeva, Brazil RLT peptide -- Esperion SCPF -- Advanced Tissue Sciences rM/NFI -- IVAX scuPA-suPAR complex - Hadasit rmCRP -- Immtech SD-9427 -- Pharmacia RN-1001 -- Renovo SDF-1 -- Ono RN-3 -- Renovo SDZ 215918 -- Novartis RNAse conjugate -- Immunomedics SDZ 280125 -- Novartis RO 631908 - Roche SDZ 89104 - Novartis Rotavirus vaccine -- Merck SDZ ABL 364 -- Novartis RP 431 -- DuPont Pharmaceuticals SDZ MMA 383 -- Novartis RP-128 -- Resolution Secretin - Ferring, Repligen RPE65 gene therapy serine protease inhibs -- Pharis RPR 110173 -- Aventis Pasteur sermorelin acetate - Serono RPR 115135 -- Aventis Pasteur SFRP-1 -- Viron RPR 116258A -- Aventis Pasteur sertenef -- Dainippon rPSGL-Ig -- American Home Products serum albumin, Recombinant human -r-SPC surfactant -- Byk Gulden Aventis Behring RSV antibody -- Medimmune serum-derived factor -- Hadasit Ruplizumab -- Biogen Sevirumab -- Novartis rV-HER-2/neu -- Therion Biologics SGN 14 - Seatle Genetics SA 1042 -- Sankyo SGN 15 -- Seatle Genetics sacrosidase - Orphan Medical SGN 17/19 -- Seatle Genetics Sant 7 SGN 30 - Seatle Genetics Sargramostim -- Immunex SGN-10 -- Seatle Genetics saruplase - Gruenenthal SGN-11 -- Seatle Genetics Satumomab -- Cytogen SH 306 -- DuPont Pharmaceuticals SB 1 -- COR Therapeutics Shanvac-B -- Shantha SB 207448 -- GlaxoSmithKline Shigella flexneri vaccine - Avant, Acambis, SB 208651 - GlaxoSmithKline Novavax SB 240683 - GlaxoSmithKline Shigella sonnei vaccine --SB 249415 -- GlaxoSmithKline

SB 249417 -- GlaxoSmithKline

SB 6 -- COR Therapeutics

sICAM-1 -- Boehringer Ingelheim

Silteplase -- Genzyme

SIV vaccine - Endocon, Institut Pasteur SK 896 -- Sanwa Kagaku Kenkyusho SK-827 -- Sanwa Kagaku Kenkyusho Skeletex -- CellFactors SKF 106160 -- GlaxoSmithKline S-nitroso-AR545C -SNTP -- Active Biotech somatomedin-1 - GroPep, Mitsubishi-Tokyo, NIH somatomedin-1 carrier protein -- Insmed somatostatin -- Ferring Somatotropin/ Human Growth Hormone -- Bio-Tech. General, Eli Lilly somatropin - Bio-Tech. General, Alkermes. SUIS-LHRH -- United Biomedical ProLease, Aventis Behring, Biovector, Cangene, Dong-A, Eli Lilly, Emisphere, Enact, Genentech, Genzyme Transgenics. YM BioSciences Novartis, Novo Nordisk, Pharmacia Serono, TranXenoGen somatropin derivative -- Schering AG somatropin, AIR -- Eli Lilly Somatropin, inhaled -- Eli Lilly/Alkermes somatropin, Kabi -- Pharmacia somatropin, Orasome -- Novo Nordisk Sonermin -- Dainippon Pharmaceutical SP(V5.2)C - Supertek SPf66 sphingomyelinase -- Genzyme SR 29001 - Sanofi SR 41476 -- Sanofi SR-29001 -- Sanofi SS1(dsFV)-PE38 -- NeoPharm ß2 microglobulin -- Avidex ß2-microglobulin fusion proteins -- NIH ß-amyloid peptides -- CeNeS ß-defensin -- Pharis Staphylococcus aureus infections --Inhibitex/ZLB

Staphylococcus aureus vaccine conjugate --Nabi Staphylococcus therapy -- Tripep Staphylokinase - Biovation, Prothera, Thrombogenetics Streptococcal A vaccine -- M6 Pharmaceuticals. North American Vaccine Streptococcal B vaccine -- Microscience Streptococcal B vaccine recombinant --Biochem Vaccines Streptococcus pyogenes vaccine STRL-33 -- NIH Subalin -- SRC VB VECTOR SUIS -- United Biomedical SUN-E3001 -- Suntory super high affinity monoclonal antibodies -Grandis/InfiMed, CSL, InfiMed, MacroMed, Superoxide dismutase - Chiron, Enzon, Ube Industries, Bio-Tech, Yeda superoxide dismutase-2 -- OXIS suppressin - UAB Research Foundation SY-161-P5 -- ThromboGenics SY-162 -- ThromboGenics Systemic lupus erythematosus vaccine --MedClone/VivoRx T cell receptor peptides -- Xoma T cell receptor peptide vaccine T4N5 liposomes -- AGI Dermatics TACI, soluble -- ZymoGenetics targeted apoptosis -- Antisoma tasonermin -- Boehringer Ingelheim TASP TASP-V Tat peptide analogues -- NIH TBP I -- Yeda TBP II TRV25H -- NIH Tc 99m ior cea1 -- Center of Molecular **Immunology** 

Tc 99m P 748 -- Diatide

TIF -- Xoma

Tifacogin - Chiron, NIS, Pharmacia

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Tissue factor -- Genentech Tc 99m votumumab -- Intracell Tissue factor pathway inhibitor Tc-99m rh-Annexin V - Theseus Imaging T.IN-135 -- Tsumura teceleukin - Biogen TM 27 -- Avant tenecteplase -- Genentech TM 29 -- Avant Teriparatide -- Armour Pharmaceuticals, TMC-151 - Tanabe Seiyaku Asahi Kasei, Eli Lilly TNF tumour necrosis factor -- Asahi Kasei terlipressin -- Ferring TNF Alpha -- Cytlmmune testisin -- AMRAD TNF antibody -- Johnson & Johnson Tetrafibricin -- Roche TNF binding protein -- Amgen TFPI -- EntreMed TNF degradation product -- Oncotech taD-IL-2 -- Takeda TNF receptor -- Immunex TGF-Alpha -- ZymoGenetics TNF receptor 1, soluble -- Amgen TGF-ß -- Kolon TNF Tumour necrosis factor-alpha -- Asahi TGF-R2 -- Insmed Kasei, Genetech, Mochida TGF-ß3 -- OSI TNF-Alpha inhibitor -- Tripep Thalassaemia gene therapy -- Crucell TNFR:Fc gene therapy - Targeted Genetics TheraCIM-h-R3 -- Center of Molecular TNF-SAM2 Immunology, YM BioSciences ToleriMab -- Innogenetics Theradigm-HBV -- Epimmune Toxoplasma gondii vaccine --Theradigm-HPV -- Epimmune GlaxoSmithKline Theradigm-malaria -- Epimmune TP 9201 - Telios Theradigm-melanoma -- Epimmune TP10 -- Avant TheraFab - Antisoma TP20 -- Avant ThGRF 1-29 -- Theratechnologies ThGRF 1-44 -- Theratechnologies tPA -- Centocor trafermin -- Scios Thrombin receptor activating peptide --TRAIL/Apo2L -- Immunex Abbott TRAIL-R1 MAb - Cambridge Antibody thrombomodulin - Iowa, Novocastra Thrombopoietin -- Dragon Pharmaceuticals, Technologies transferrin-binding proteins -- CAMR Genentech Transforming growth factor-beta-1 -thrombopoietin, Pliva -- Receptron Genentech Thrombospondin 2 transport protein -- Genesis thrombostatin -- Thromgen Trastuzumab -- Genetech thymalfasin -- SciClone TRH -- Ferring thymocartin – Gedeon Richter Triabin -- Schering AG thymosin Alpha1 -- NIH thyroid stimulating hormone -- Genzyme Triconal Triflavin tICAM-1 -- Bayer troponin I -- Boston Life Sciences Tick anticoagulant peptide -- Merck TRP-2" -- NIH

FIG. 28BB

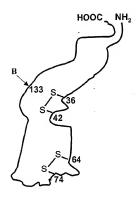
trypsin inhibitor -- Mochida

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Vascular endothelial growth factors - R&D TSP-1 gene therapy -Systems TT-232 vascular targeting agents -- Peregrine TTS-CD2 -- Active Biotech vasopermeation enhancement agents --Tuberculosis vaccine -- Aventis Pasteur. Peregrine Genesis Tumor Targeted Superantigens -- Active vasostatin -- NIH Biotech -- Pharmacia VCI -- Bio-Tech, General VEGF - Genentech. Scios tumour vaccines -- PhotoCure tumour-activated prodrug antibody VEGF inhibitor -- Chugai VEGF-2 -- Human Genome Sciences conjugates -- Millennium/ImmunoGen VEGF-Trap -- Regeneron tumstatin -- ILEX viscumin, recombinant -- Madaus Tuvirumab -- Novartis Vitaxin TV-4710 - Teva Vitrase - ISTA Pharmaceuticals TWEAK receptor -- Immunex West Nile virus vaccine -- Bavarian Nordic TXU-PAP WP 652 TY-10721 - TOA Eiyo Type I diabetes vaccine -- Research Corp WT1 vaccine -- Corixa WX-293 -- Wilex BioTech. Typhoid vaccine CVD 908 WX-360 -- Wilex BioTech. U 143677 -- Pharmacia WX-LIK1 -- Wilex BioTech. U 81749 -- Pharmacia XMP-500 - XOMA UA 1248 -- Arizona XomaZvme-791 -- XOMA UGIF -- Sheffield XTL 001 -- XTL Biopharmaceuticals UIC 2 XTL 002 -- XTL Biopharmaceuticals UK 101 veast delivery system -- Globelmmune UK-279276 - Corvas Intl. Yersinia pestis vaccine urodilatin -- Pharis YIGSR-Stealth -- Johnson & Johnson urofollitrophin -- Serono Yissum Project No. D-0460 -- Yissum Urokinase -- Abbott YM 207 - Yamanouchi uteroferrin-- Pepgen YM 337 -- Protein Design Labs V 20 -- GLYCODesign Yttrium-90 labelled biotin V2 vasopressin receptor gene therapy Yttrium-90-labeled anti-CEA MAb T84.66 vaccines -- Active Biotech 7D 0490 - AstraZeneca Varicella zoster glycoprotein vaccine -Research Corporation Technologies ziconotide -- Elan Varicella zoster virus vaccine live -- Cantab ZK 157138 -- Berlex Laboratories Pharmaceuticals Zolimomab aritox Vascular endothelial growth factor -Zorcell -- Immune Response

Genentech, University of California

ZRXL peptides - Novartis



$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_b \\ -\mathrm{GalNAc\text{-}(Gal)_a\text{-}(Sia)_c\text{-}} (R)_d \end{pmatrix}_e$$

a-c, e (independently selected) = 0 or 1; d = 0;  $R = modifying\ group,\ sialyl\ or \ oligosialyl$ 

FIG. 29A

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CHO, BHK, 293 cells, Vero expressed G-CSF a-c, e (independently selected) = 0 or 1; d = 0

1. Sialidase 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 29B

Insect cell expressed G-CSF a, e (independently selected) = 0 or 1;

b, c, d = 0.

1. Galactosyltransferase, UDP-Gal 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 29C

```
E. coli expressed G-CSF
a-e = 0.
```

GalNAc Transferase, UDP-GalNAc
 CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

### FIG. 29D

```
NSO expressed G-CSF
a, e (independently selected) = 0 or 1;
b, c, d = 0
```

```
1. CMP-SA-levulinate, ST3Gal1

2. H<sub>4</sub>N<sub>2</sub>-PEG
```

a, c, d, e (independently selected) = 0 or 1; b = 0; R = PEG.

#### FIG. 29E

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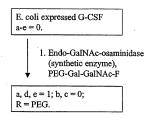


FIG. 29F

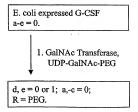
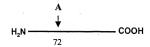


FIG. 29G



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & & \\ | & &$$

a-d, i, n-u (independently selected) = 0 or 1. aa, bb, cc, dd, ee (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z = 0; R = modifying group, mannose, oligo-mannose. R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 30A

```
GHO, BHK, 293 cells, Vero expressed interferon alpha 14C.
a-d, aa, bb = 1; e-h = 1 to 4;
cc, j-m, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0.
```

Sialidase
 CMP-SA-PEG, ST3Gal3

```
a-d, aa, bb = 1; e-h = 1 to 4;
bb, cc, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0;
v-y (independently selected) = 1,
when j-m (independently selected) = 1;
R = PEG.
```

#### FIG. 30B

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-q, s, u, v-z, cc, dd, ee = 0; e, g, i, r, t (independently selected) = 0 or 1; aa, bb = 1.
```

GNT's 1&2, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-PEG

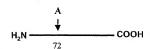
```
b, d, f, h, j-q, s, u, w, y, z, cc, dd, ee = 0;
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when a, c, (independently selected) = 1;
aa, bb = 1; R = PEG.
```

Yeast expressed interferon alpha-14C.
a-q, cc, dd, ee, v-z = 0;
r-y (independently selected) = 0 to 1;
aa, bb = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

Endo-H
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

a-z, bb=0; aa=1; R'=-Gal-Sia-PEG.

FIG. 30D



$$(Fuc)_{i} \\ \mathbf{A} \leftarrow \begin{matrix} (Glc)_{a} \\ Glc)_{d} \\ Glc)_{d} \\ Glc)_{d} \\ (R')_{d} \end{matrix} \\ (Glc)_{d} \\ (Glc)_{d}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1. R = polymer; R' = sugar, glycoconjugate.

FIG. 30E

### 68/498

```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

# 1. CMP-SA-PEG, ST3Gal3 ▼

```
h=1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z=1; n=0; R=PEG.
```

#### FIG. 30F

```
Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- GNT's 1,2,4,5, UDP-GlcNAc
   Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

#### FIG. 30G

# 69/498

Yeast expressed interferon alpha-14C. a-n=0; r-y (independently selected) = 0 to 1; z=1; R (branched or linear) = Man, oligomannose.

```
1. mannosidases
```

- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

### FIG. 30H

NSO expressed interferon alpha 14C. a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

> CMP-SA-levulinate, ST3Gal3, buffer, salt
>  H<sub>4</sub>N<sub>2</sub>-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 301

# 70/498

CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA-PEG, α2,8-ST

h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.

### FIG. 30J

CHO, BHK, 293 cells, Vero expressed Interferon alpha-14C. a-g, j-m, r-u (independently selected) = 0 or 1; h = 1 to 3; n, v-y = 0; z = 1.

Sialidase
 Trans-sialidase, PEG-Sia-lactose

 $\begin{array}{lll} a\text{-g, j-m, r-y} & (independently selected) = 0 \ or \ 1; \\ h=1 \ to \ 3; \ n=0; \ z=1; \ R=PEG. \end{array}$ 

### FIG. 30K

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA, α2,8-ST

h = 1 to 3;
```

a-g, i, r-u (independently selected) = 0 or 1; j-m (independently selected) = 0 to 40;

### FIG. 30L

z = 1; v-y, n = 0.

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

```
    GNT's 1 & 2, UDP-GlcNAc
    Galactosyltransferase,
    UDP-Gal-linker-SA-CMP
    ST3Gal3, transferrin
```

```
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1; z = 1; b, d, f, h, j-n, s, u, w, y = 0; R = \text{transferrin}.
```

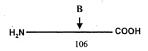
### FIG. 30M

Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.

endoglycanase
 Galactosyltransferase,
 UDP-Gal-linker-SA-CMP
 ST3Gal3, transferrin

i (independently selected) = 0 or 1; a-h, j-m, r-z = 0; n = 1; R' = -Gal-linker-transferrin.

FIG. 30N



a-c, e, f (independently selected) = 0 or 1; d, g = 0; R = polymer, glycoconjugate.

FIG. 300

CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c (independently selected) = 0 or 1; e=1; d, f, g=0

1. Sialidase
2. CMP-SA-PEG, ST3Gal1

a-d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

### FIG. 30P

Insect cell expressed interferon alpha (2a or 2b). a, e (independently selected) = 0 or 1; b, c, d, f, g = 0.

Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; b, f, g = 0; R = PEG.

FIG. 30Q

## 75/498

E. coli expressed IF-alpha (2a or 2b). a-g = 0.

GalNAc Transferase,
 UDP-GalNAc-PEG

a-c, f, g = 0; d, e = 1; R = PEG.

## FIG. 30R

NSO expressed IF-alpha (2a or 2b). a (independently selected) = 0 or 1;

e = 1; b, c, d, f, g = 0

1. CMP-SA-levulinate, ST3Gal1

2. H<sub>4</sub>N<sub>2</sub>-PEG

a, c, d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 30S

E. coli expressed IF-alpha (2a or 2b). a-g = 0.

 Endo-N-acetylgalatosamidase (synthetic enzyme), PEG-Gal-GalNAc-F

a, d, e = 1; b, c, f, g = 0; R = PEG.

### FIG. 30T

E. coli expressed IF-alpha (2a or 2b). a-g=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. sialyltransferase, CMP-SA-PEG

b, d = 0 or 1; e = 1; a, c, f, g = 0; R = PEG.

FIG. 30U

## 77/498

```
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c, f (independently selected) = 0 or 1; e=1; d, g=0
```

Sialidase
 CMP-SA-PEG, ST3Gal1 and ST3Gal3

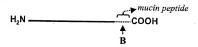
a-d, f, g (independently selected) = 0 or 1; e = 1; R = PEG.

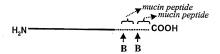
#### **FIG. 30V**

```
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c, f (independently selected) = 0 or 1;
e = 1; d, g = 0
```

- 1. Sialidase
  2. CMP-SA-linker-SA-CMP,
  ,ST3Gal1
  3. ST3Gal3, transferrin
- a-d, f (independently selected) = 0 or 1; e = 1; R = transferrin; g = 0.

#### FIG. 30W





$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_b \\ -(\operatorname{GalNAc-(Gal)_a-(Sia)_c-(R)_d})_c \end{pmatrix}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, glycoconjugate.

FIG. 30X

### 79/498

CHO, BHK, 293 cells, Vero expressed interferon alpha-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

- Sialidase
   CMP-SA-PEG, ST3Gal1
- a-d, e (independently selected) = 0 or 1; R = PEG.

#### FIG. 30Y

Insect cell expressed interferon alpha-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 30Z

## 80/498

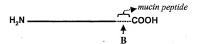
E. coli expressed interferon alpha-mucin fusion protein.

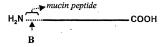
a-e = 0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 30AA





$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_b \\ -\operatorname{GalNAc-(Gal)_a-(Sia)_c-(R)_d} \end{pmatrix}$$

$$C \leftarrow (R')_n$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 30BB

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

#### FIG. 30CC

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

- GalNAc Transferase,
   UDP-GalNAc-linker-SA-CMP
   ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 30DD

E. coli expressed Interferon alpha (no fusion). a-e, n = 0.

NHS-CO-linker-SA-CMP
 ST3Gal3, transferrin

a-e = 0; n = 1; R' = linker-transferrin.

FIG. 30EE

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$$(Fuc)_{i} \\ \mathbf{A} \leftarrow \underbrace{\mathsf{GlcNAc}}_{l} \\ \mathsf{GlcNAc} - \underbrace{\mathsf{GlcNAc}}_{l} \\ \mathsf{GlcNAc} - \underbrace{\mathsf{GlcNAc}}_{l} \\ \mathsf{GlcNAc} - \underbrace{\mathsf{GlcNAc}}_{l} \\ \mathsf{A} \leftarrow \underbrace{\mathsf{GlcNAc}}_{l} \\ \mathsf{GlcNAc} - \underbrace{\mathsf{Gal}}_{l} \\ \mathsf{al}_{l} \\$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer

FIG. 31A

## 85/498

CHO, BHK, 293 cells, Vero expressed IF-beta h=1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.

Sialidase
 CMP-SA-PEG, ST3Gal3

h=1 to 3; a-g, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; j-m, v-y (independently selected) = 0 or 1; z=1; n=0; R=PEG.

## FIG. 31B

Insect cell expressed IF-beta a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.

 GNT's 1&2, UDP-GIcNAc
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3, buffer, salt

 $\label{eq:continuous} \begin{array}{ll} b,\,d,\,f,\,h,\,k,\,m,\,n,\,s,\,u,\,w,\,y=0;\\ a,\,c,\,e,\,g,\,i,\,r,\,t\ \ (independently\ selected)=0\ \ or\ 1;\\ j,\,l,\,v,\,x\ \ (independently\ selected)=0\ \ or\ 1;\\ z=1;\ R=PEG. \end{array}$ 

#### FIG. 31C

```
Yeast expressed IF-beta
a-n = 0; z = 1;
r-y (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose or polysaccharide.
```

```
1. Endo-H
```

2. Galactosyltransferase, UDP-Gal

↓ 3.. CMP-SA-PEG, ST3Gal3

a-m, r-z=0; n = 1; R' = -Gal-Sia-PEG.

## FIG. 31D

```
CHO, BHK, 293 cells, Vero expressed IF-beta h=1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z=1.
```

1. CMP-SA-PEG, ST3Gal3

```
\begin{array}{l} h=1 \text{ to 3;} \\ a\text{-g, i (independently selected)} = 0 \text{ or 1;} \\ r\text{-u (independently selected)} = 0 \text{ or 1;} \\ j\text{-m, v-y (independently selected)} = 0 \text{ or 1;} \\ z=1; \text{ n=0; } R=PEG. \end{array}
```

#### FIG. 31F

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$$\label{eq:continuous} \begin{split} &\text{Insect cell expressed IF-beta} \\ &\text{a-d, f, h, j-n, s, u, v-y=0; e, g, i, r, t} \\ &\text{(independently selected)=0 or 1; } z=1. \end{split}$$

GNT's 1,2,4,5, UDP-GleNAc
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1: n = 0: R = PEG.

#### FIG. 31F

Yeast expressed IF-beta a-n=0; z=1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

## 88/498

```
NSO expressed IF-beta
a-i, r-u (independently selected) = 0 or 1;
j-m, n, v-y = 0; z = 1.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG
a-i, j-m, r-y (independently selected) = 0 or 1;
n = 0; z = 1; R = PEG.
```

## FIG. 31H

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, α2,8-ST

```
\begin{split} &h=1\ to\ 3;\\ &a\cdot g,\ i,\ r\cdot u\ (independently\ selected)=0\ or\ 1;\\ &j\cdot m\ (independently\ selected)=0\ to\ 2;\\ &v\cdot y\ (independently\ selected)=1,\\ &when\ j\cdot m\ (independently\ selected)\ is\ 2;\\ &z=1;\ n=0;\ R=PEG. \end{split}
```

#### FIG. 311

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CHO, BHK, 293 cells, Vero expressed IF-beta a-g, j-m, r-u (independently selected) = 0 or 1; h=1 to 3; n, v-y=0; z=1.

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

#### FIG. 31J

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- Sialidase
  - 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
  - 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n=0;

v-y (independently selected) = 0 or 1; R = PEG.

FIG. 31K

### 90/498

```
NSO expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0;
Sia (independently selected) = Sia or Gal.
```

- Sialidase and α-galactosidase
   α-Galactosyltransferase, UDP-Gal
   3. CMP-SA-PEG, ST3Gal3
- a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; R = PEG n = 0; v-y (independently selected) = 1, when j-m (independently selected) is 1;

#### FIG. 31L

```
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.
```

- Sialidase
   CMP-SA-PEG (16 mol eq), ST3Gal3
   CMP-SA, ST3Gal3
- a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n = 0; v-y (independently selected) = 0 or 1; R = PEG.

## FIG. 31M

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H<sub>4</sub>N<sub>2</sub>-PEG

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n = 0; v-y (independently selected) = 0 or 1; R = PEG.

## FIG. 31N

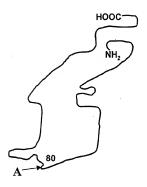
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

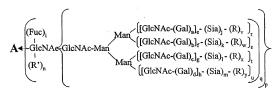
1. CMP-SA, α2,8-ST

a-d, i, r-u, z (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; n, v-y (independently selected) = 0.

FIG. 310

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a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group; R' = H, glycosyl group, modifying group, glycoconjugate.

FIG. 31P

### 93/498

```
Insect cell expressed Ifn-beta.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

#### FIG. 31Q

```
Yeast expressed Ifin-beta. 
a-m = 0; q-y (independently selected) = 0 to 1; p = 1; 
R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
  2. Galactosyltransferase, UDP-Gal

  3. CMP-SA-PEG, ST3Gal3
- a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

#### FIG. 31R

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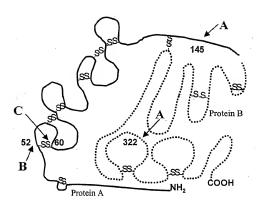
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

- CMP-SA-linker-SA-CMP, ST3Gal3
   ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-transferrin.

FIG. 31S

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$$\mathbf{A} \leftarrow \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_a]_c^-}(\operatorname{Sia})_j - (R)_v \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_c^-}(\operatorname{Sia})_j - (R)_w \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_c^-}(\operatorname{Sia})_j - (R)_x \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_g^-}(\operatorname{Sia})_j - (R)_x \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_g^-}(\operatorname{Sia})_m - (R)_y \end{bmatrix}_u \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_g^-}(\operatorname{Sia})_m - (R)_y \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_g^-}(\operatorname{Sia})_m - (R)_y \end{bmatrix}_u \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_g^-}(\operatorname{Sia})_m - (R)_y \end{bmatrix}_t \\ = \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_b]_g^-}(\operatorname{Sia})_m -$$

 $\mathbf{B} \leftarrow \left( \text{Glc-}(\mathbf{X}\mathbf{y}\mathbf{l})_{n} \right)_{0}$ 

**C ←**[-Fuc]<sub>n</sub>

a-d, i, q-u (independently selected) = 0 or 1. o, p (independently selected) = 0 or 1. e-h, n (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-y = 0;

R = modifying group, mannose, oligomannose, Sia-Lewis X, Sia-Lewis A...

FIG. 32A

# 96/498

```
BHK expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.
```

```
    Sialidase
    CMP-SA-PEG (16 mole eq),
ST3Gal3
```

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4; v, x, (independently selected) = 1, when j, l (respectively, independently selected) is 1; R = PEG.
```

#### FIG. 32B

CHO, BHK, 293 cells, Veto expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

```
    Sialidase
    CMP-SA-PEG (1.2 mole eq),
ST3Gal3
    CMP-SA (8 mol eq), ST3Gal3
```

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4; v or x, (independently selected) = 1, when j or l, (respectively, independently selected) is 1; R = PEG.
```

#### FIG. 32C

# 97/498

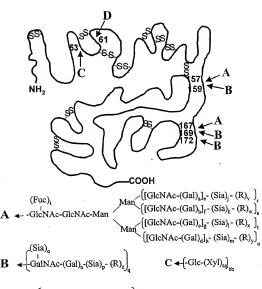
NSO expressed Factor VII or VIIa a--u (independently selected) = 0 or 1; v-y = 0; n = 0-4; Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

a-m, o-u (independently selected) = 0 or 1; n = 0.4; v-y (independently selected) = 1, when j-m (independently selected) is 1; Sia = Sia; R = PEG.

FIG. 32D





D ←-Fuc (GlcNAc)<sub>cc</sub>-(Gal)<sub>dd</sub>-(Sia)<sub>eg</sub> (R)<sub>gg</sub>

a-d, i, n-u (independently selected) = 0 or 1. bb, cc, dd, ec, ff, gg (independently selected) = 0 or 1. e-h, aa (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z = 0: R = modifying group, mannose, oligo-mannose,

**FIG. 33A** 

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CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q=1; e-h=1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg=0.

Sialidase

2. CMP-SA-PEG, ST3Gal3

a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; o, p, z = 0; j-m, ee, v-y, gg (independently selected) = 0 or 1; R = PEG.

#### FIG. 33B

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

Sialidase

CMP-SA-PEG, ST3Gal3

3. ST3Gal1, CMP-SA

a-d, n, p, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1; j-m, ee, v-y, gg (independently selected) = 0 or 1; o, z = 0; R = PEG.

#### FIG. 33C

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

```
    sialidase
```

- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
  4. CMP-SA-PEG, ST3Gal1

```
a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1; R = PEG;
o, v-y, gg = 0;
j-m, p, ee (independently selected) = 0 or 1, but when p = 1, z = 1.
```

### FIG. 33D

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q=1; e-h=1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; R = PEG;
o, p, z = 0; j-m, ee, v-y, gg (independently selected) = 0 or 1.
```

#### FIG. 33E

### 101/498

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q=1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H<sub>4</sub>N<sub>2</sub>-PEG

a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; o, p, z = 0; R = PEG; j-m, ee, v-y, gg (independently selected) = 0 or 1.

#### FIG. 33F

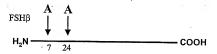
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; e-, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

1. CMP-SA-PEG, α2,8-ST

a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; o, p, z = 0; R= PEG; j-m, ee (independently selected) = 0 to 2; v-y, gg (independently selected) = 1, when j-m (independently selected) is 2;

#### FIG. 33G





$$\mathbf{A} \leftarrow \underbrace{ \begin{aligned} & \text{[GlcNAc-(Gal)_a]_c^-(Sia)_j^-(R)_v} \\ & \text{[GlcNAc-Gal)_b]_t^-(Sia)_k^-(R)_w} \\ & \text{[GlcNAc-Gal)_b]_t^-(Sia)_k^-(R)_w} \\ & \text{[GlcNAc-(Gal)_b]_g^-(Sia)_j^-(R)_w} \\ & \text{[[GlcNAc-(Gal)_d]_g^-(Sia)_m^-(R)_y]_u} \end{aligned} }_{\mathbf{Man}}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose.

**FIG. 34A** 

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

# FIG. 34B

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. Sialidase
  - CMP-SA-PEG (1.2 mol eq), ST3Gal3
  - 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34C

NSO expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.

- Sialidase and α-galactosidase
   Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

#### FIG. 34D

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase 2. CMP-SA-PEG (16 mol eq),
- ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

#### FIG. 34E

### 105/498

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H<sub>2</sub>N<sub>2</sub>-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

## FIG. 34F

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 34G

Insect cell expressed FSH. a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.

> 1. GNT's 1,2,4,5, UDP-GlcNAc 2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1: j-m=0; v-y (independently selected) = 1. when e-h (independently selected) is 1; R = PEG

### FIG. 34H

Yeast expressed FSH. a-m=0; q-y (independently selected) = 0 to 1; p = 1: R (branched or linear) = Man, oligomannose.

- Endoglycanase 2. Galactosyltransferase, UDP-Gal ◆ 3. CMP-SA-PEG, ST3Gal3
- a-m, p-y = 0;

 $n ext{ (independently selected)} = 0 ext{ or } 1;$ R' = -Gal-Sia-PEG.

#### FIG. 341

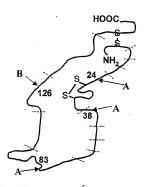
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

 CMP-SA-linker-SA-CMP, ST3Gal3
 ST3Gal1, desialylated chorionic gonadrophin (CG) produced in CHO.
 CMP-SA, ST3Gal3, ST3Gal1

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-CG.

FIG. 34J

## 108/498



$$\begin{array}{c} (\operatorname{Fuc})_{i} \\ \mathbf{A} & \leftarrow -\operatorname{GlcNAc-GlcNAc-Man} \\ & \left[ (\operatorname{GlcNAc-Gal})_{a} \right]_{e}^{-} (\operatorname{Sia})_{p}^{-} (R)_{v} \right]_{r} \\ & \left[ (\operatorname{GlcNAc-Gal})_{a} \right]_{e}^{-} (\operatorname{Sia})_{r}^{-} (R)_{v} \right]_{s} \\ & \left[ (\operatorname{GlcNAc-Gal})_{d} \right]_{e}^{-} (\operatorname{Sia})_{r}^{-} (R)_{v} \right]_{u} \\ & \mathbf{B} & \left( -\operatorname{Gal})_{A} \right]_{e}^{-} (\operatorname{Sia})_{p}^{-} (R)_{z} \\ & \left[ (\operatorname{GlcNAc-(Gal)}_{d} \right]_{h}^{-} (\operatorname{Sia})_{m}^{-} (R)_{y} \right]_{u} \\ \end{array}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z=0; R = polymer.

FIG. 35A

## 109/498

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to1; v-z=0
```

2. CMP-SA-PEG, ST3Gal3

1. Sialidase

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

#### FIG. 35B

```
Insect cell expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.
```

GNT's 1&2, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

 $\begin{array}{l} b,\,d,\,f,\,h,\,k,\,m\text{-}q,\,s,\,u,\,w,\,y,\,z=0;\\ a,\,c,\,e,\,g,\,i,\,r,\,t\ \ (independently\ selected)=0\ or\ 1;\\ j,\,l,\,v,\,x\,(independently\ selected)=0\ or\ 1;\\ R=PEG. \end{array}$ 

#### FIG. 35C

# 110/498

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z=0.

- sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- ↓ 4. CMP-SA-PEG, ST3Gal1

```
a-h, n, q = 1;
i-m, o, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

### FIG. 35D

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h=1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z=0
```

1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

#### FIG. 35E

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

GNT's 1, 2 & 5, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-PEG

a-c, e-g, i, i-t, v-x (independently selected) = 0 or 1; d, h, i-q, u, y, z = 0; R = PEG.

## FIG. 35F

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- GNT's 1, 2 & 5, UDP-GlcNAc
   Galactosidase (synthetic enzyme),
   PEG-Gal-F
- a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 35G

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z=0; e, g, i, r, t (independently selected) = 0 or 1.

1. GNT-1, UDP-GlcNAc-PEG

e, i, r, v (independently selected) = 0 or 1; a-h, j-q, s-u, w-z = 0; R = PEG.

## FIG. 35H

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z=0; e, g, i, r, t (independently selected) = 0 or 1.

- GNT-1, UDP-GlcNAc
  - 2. Galactosyltransferase, UDP-Gal-PEG

a, e, i, r, v (independently selected) = 0 or 1; b-d, f-h, j-q, s-u, w-z = 0; R = PEG.

FIG. 351

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- GNT-1, UDP-GlcNAc
   Galactosyltransferase, UDP-Gal
   ST3Gal3, CMP-SA-PEG

a, e, i, j, r, v (independently selected) = 0 or 1; b-d, f-h, k-q, s-u, w-z = 0; R = PEG.

## FIG. 35J

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- Galactosyltransferase, UDP-Gal
  - 3. ST3Gal3, CMP-SA-PEG

a-c, e-g, i-l, r-t, v-x (independently selected) = 0 or 1; d, h, m-q, u, y, z = 0; R = PEG.

FIG. 35K

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- GNT's 1, 2 & 5, UDP-GlcNAc
   Galactosyltransferase, UDP-Gal
- ▼ 3. α2,6-sialyltransferase, CMP-SA-PEG

```
a-c, e-g, i-l, r-t, v-x (independently selected)
= 0 or 1;
d, h, m-q, u, y, z = 0; R = PEG.
```

## FIG. 35L

```
CHO, BHK, 293 cells, Vero expressed EPO
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.

1. sialidase
2. CMP-SA, ST3Gal3
3. CMP-SA-PEG, ST3Gal1
```

```
a-h, q, i-o, r-u (independently selected)
= 0 or 1;
v-y=0; p, z=0 or 1; R=PEG.
```

#### FIG. 35M

## 115/498

```
CHO, BHK, 293 cells, Vero expressed EPO
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, q-u (independently selected) = 0 or 1;
```

R = PEG.

y-y=0; p, z=0 or 1;

# FIG. 35N

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG,  $\alpha$ 2,8-sialyltransferase

FIG. 350

# 116/498

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

CMP-SA-PEG, α2,8-sialyltransferase

a-h, i-o, p-u, v-z (independently selected) = 0 or 1; R = SA-PEG.

#### FIG. 35P

yeast or fungi expressed EPO r, t, u, v, x, y (independently selected) = 0 or 1; a-m, n-q, s, w, z = 0; R = (Man)<sub>n</sub> where n = 1-5, linear or branched.

- mannosidases
   GNT-1, UDP-GlcNAc
   galactosyltransferase, UDP-Gal
   ST3Gal3, CMP-SA-PEG
- a, e, j, r, v (independently selected) = 0 or 1; b-d, f-i, k-q, s-u, w-z = 0; R = PEG.

FIG. 35Q

# 117/498

yeast or fungi expressed EPO r, t, u, v, x, y (independently selected) = 0 or 1; a-m, n-q, s, w, z = 0;  $R = (Man)_n$  where n = 1-5, linear or branched.

mannosidases
 GNT-1, UDP-GlcNAc-PEG

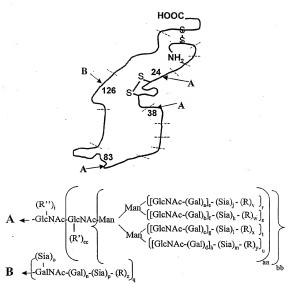
e, r, v (independently selected) = 0 or 1; a-h, i-q, s-u, w-z = 0; R = PEG.

### FIG. 35R

yeast or fungi expressed EPO r, t, u, v, x, y (independently selected) = 0 or 1; a-m, n-q, s, w, z = 0;  $R = (Man)_n$  where n = 1-5, linear or branched.

- mannosidase-I
   GNT-1, UDP-GlcNAc
   galactosyltransferase, UDP-Gal
   ST3Gal3, CMP-SA-PEG
- a, e, j, r, t-u, v, x, y (independently selected) = 0 or 1; b-d, f-i, k-q, s, w, z = 0;  $(R)_v = PEG$ ;  $(R)_x$  and  $(R)_y = Man$ .

### FIG. 35S



a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20.

v-z=0; aa, bb=1; cc=0;

R = polymer; R" and R' = sugar-polymer or Fuc.

FIG. 35T

```
yeast or fungi expressed EPO

r, t, u, v, x, y (independently selected) = 0 or 1;

cc, a-m, n-q, s, w, z = 0;

aa, bb = 1;

R = (Man)_a where n = 1-100, linear or branched.
```

```
    1. endo-H
    2. galactosyltransferase, UDP-Gal-PEG
```

```
i (independently selected) = 0 or 1;
aa, bb, cc, a-h, j-z = 0; R" = Gal-PEG.
```

#### FIG. 35U

```
yeast or fungi expressed EPO r, t, u, v, x, y (independently selected) = 0 or 1; cc, a-m, n-q, s, w, z = 0; aa, bb = 1; R = (Man)_n where n = 1-100, linear or branched.
```

- endo-H
   galactosyltransferase, UDP-Gal
- 3. ST3Gal3, CMP-SA-PEG

```
i (independently selected) = 0 or 1;
aa, bb, cc, a-h, j-z=0; R" = Gal-SA-PEG.
```

### FIG. 35V

# 120/498

```
Insect cell expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1; aa = 1; \mathbb{R}^{2} = Fuc.
```

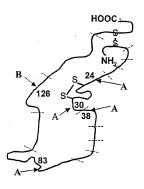
mannosidases

2. galactosyltransferase, UDP-Gal-PEG

cc, e, i, r, v (independently selected) = 0 or 1; bb, a-h, j-q, s-u, w-z = 0; aa = 1; R' = Gal-PEG.

FIG. 35W

# 121/498



$$\begin{array}{c} (\operatorname{Fuc})_i \\ \mathbf{A} \leftarrow -\operatorname{GlcNAc-GlcNAc-Man} \\ & \begin{array}{c} \operatorname{Man} \left[ [\operatorname{GlcNAc-(Gal)}_a]_e \cdot (\operatorname{Sia})_i \cdot (R)_v \right]_e \\ [\operatorname{GlcNAc-(Gal)}_b]_f \cdot (\operatorname{Sia})_k \cdot (R)_w \right]_e \\ & \begin{array}{c} \operatorname{Man} \left[ [\operatorname{GlcNAc-(Gal)}_b]_g \cdot (\operatorname{Sia})_f \cdot (R)_v \right]_e \\ (\operatorname{GlcNAc-(Gal)}_d]_h \cdot (\operatorname{Sia})_m \cdot (R)_y \right]_u \\ \\ \mathbf{B} \leftarrow \left( \begin{array}{c} \operatorname{Gial}_b \cdot (\operatorname{Gal})_m \cdot (\operatorname{Sia})_p \cdot (R)_z \\ -\operatorname{GalNAc-(Gal)}_m \cdot (\operatorname{Sia})_p \cdot (R)_z \right)_q \\ \\ & \begin{array}{c} \operatorname{a-d}, \ i, \ n-u \ (independently \ selected) = 0 \ \text{to} \ 4. \end{array} \right. \end{array}$$

a-d, i, n-ti (independently selected) = 0 or 1 e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer.

FIG. 35X

## 122/498

```
NSO expressed NESP q = 1; a-i, n, r-u (independently selected) = 0 or 1; j-m, o, p, v-z = 0
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-PEG
```

```
q = 1; a-i, j-n, r-y (independently selected) = 0 or 1;
o, p, z = 0; R = PEG.
```

# FIG. 35Y

```
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z=0
```

### 1. CMP-SA-PEG, α2,8-ST

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG; z = 0.
```

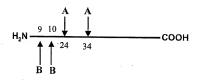
#### FIG. 35Z

CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0

1 CMP-SA, poly- $\alpha$ 2,8-ST

a-g, n, q = 1; h = 1 to 3; i, j-m, o, p, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-40; R = Sia.

FIG. 35AA



$$\begin{array}{c} \textbf{A} & \longleftarrow \\ (\text{Fuc})_{i} \\ -\text{GlcNAc-GlcNAc-Man} \\ & \boxed{ \begin{bmatrix} [\text{GlcNAc-(Gal)}_{a}]_{e^{-}} (\text{Sia})_{j}^{-} (R)_{v} \end{bmatrix}_{r} \\ \left[ [\text{GlcNAc-(Gal)}_{b}]_{l^{-}} (\text{Sia})_{k}^{-} (R)_{w} \end{bmatrix}_{r} \\ Man \\ \left[ [\text{GlcNAc-(Gal)}_{d}]_{g^{-}} (\text{Sia})_{l^{-}} (R)_{x} \end{bmatrix}_{t} \\ \left[ [\text{GlcNAc-(Gal)}_{d}]_{h^{-}} (\text{Sia})_{m^{-}} (R)_{y} \end{bmatrix}_{u} \\ \end{array}$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{o} \\ -(\operatorname{GalNAc-(Gal})_{n}-(\operatorname{Sia})_{p}-(R)_{g} \end{bmatrix}_{2a}$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 36A

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.
```

 Sialidase
 CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

#### FIG. 36B

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.
```

- Sialidase
- 2. CMP-SA-PEG (1.2 mol eq),

7 3. CMP-SA (16 mol eq), ST3Gal3 & ST3Gal1

a-d, i-m, p-u, as (independently selected) = 0 or 1; o, z = 0; n, e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

#### FIG. 36C

```
NSO expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z=0;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-PEG, ST3Gal1

```
a-d, i-m, p-u, z, aa (independently selected) = 0 or 1;
n, e-h = 1; o, v-y = 0; z = 1, when p = 1; R = PEG.
```

#### FIG. 36D

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.
```

- 1. Sialidase
- CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-y, aa (independently selected) = 0 or 1; o, p, z = 0; n, e-h = 1; R = PEG.
```

#### FIG. 36E

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H<sub>4</sub>N<sub>2</sub>-PEG

a-d, i-m, o-y, aa (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = PEG.

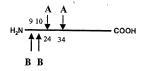
#### FIG. 36F

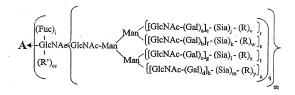
CHO, BHK, 293 cells, Vero expressed GMCSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

1. CMP-SA, α2,8-ST

a-d, i, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; j-m (independently selected) = 0-20; v-z (independently selected) = 0.

FIG. 36G





$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{pmatrix}_{aa}$$

a-d, i, n-u, aa, bb, cc (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group. glycoconjugate.

FIG. 36H

# 129/498

```
Insect cell expressed GM-CSF.
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, n, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

#### FIG. 361

```
Yeast expressed GM-CSF.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

```
    Endoglycanase
    mannosidase (if aa = 1).
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-p, r-z, aa, bb = 0;
q, cc (independently selected) = 0 or 1;
R' = -Gal-PEG.
```

FIG. 36J

CHO, BHK, 293 cells, Vero expressed GM-CSF. a--m, o-u, aa, bb (independently selected) = 0 or 1; n, v-z, cc = 0.

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-linker-SA-CMP, ST3Gal1
- 3. ST3Gal3, transferrin

a--m, p-u, z, as (independently selected) = 0 or 1; o, v-y, cc = 0; bb, n = 1; R = transferrin.

FIG. 36K



$$\mathbf{A} \leftarrow \begin{bmatrix} \operatorname{Fuc})_{i} & \operatorname{Man} & \left[ [\operatorname{GlcNAc-(Gal)_{a}]_{e^{-}}} (\operatorname{Sia})_{j^{-}} (\operatorname{R})_{v} \right]_{r} \\ \operatorname{GlcNAc-GlcNAc-Man} & \operatorname{Man} & \left[ [\operatorname{GlcNAc-(Gal)_{b}]_{f^{-}}} (\operatorname{Sia})_{i^{-}} (\operatorname{R})_{w} \right]_{s} \\ \operatorname{Man} & \left[ [\operatorname{GlcNAc-(Gal)_{d}]_{g^{-}}} (\operatorname{Sia})_{i^{-}} (\operatorname{R})_{x} \right]_{t} \\ \left[ [\operatorname{GlcNAc-(Gal)_{d}]_{h^{-}}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \right]_{u} \\ \end{bmatrix}_{q} \end{aligned}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 37A

# 132/498

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
1. Sialidase
2. CMP-SA-PEG (16 mol eq),
5T3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

## FIG. 37B

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

```
1. Sialidase
2. CMP-SA-PEG (1.2 mol eq),
ST3Gal3
```

3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

### FIG. 37C

# 133/498

```
NSO expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
```

- Sialidase and α-galactosidase
   α-Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

#### FIG. 37D

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
    CMP-SA, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

## FIG. 37E

# 134/498

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
1. CMP-SA-levulinate, ST3Gal3, 2. H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R \doteq PEG.
```

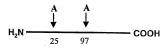
#### FIG. 37F

```
CHO, BHK, 293 cells, Vero expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

# 1. CMP-SA, α2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

#### FIG. 37G



$$\mathbf{A} \leftarrow \begin{bmatrix} \text{Fuc})_i \\ \text{GlcNAc-GlcNAc-Man} \\ \text{R'})_n \end{bmatrix} \begin{bmatrix} \text{[GlcNAc-(Gal)_a]_s- (Sia)_j - (R)_v} \\ \text{[GlcNAc-(Gal)_b]_r- (Sia)_k - (R)_w} \end{bmatrix}_s \\ \text{[GlcNAc-(Gal)_a]_s- (Sia)_j - (R)_x} \end{bmatrix}_t \\ \text{[GlcNAc-(Gal)_d]_s- (Sia)_m - (R)_y} \end{bmatrix}_q \\ \text{[GlcNAc-(Gal)_d]_s- (Sia)_m - (R)_y} \\ \text{[GlcNA$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 37H

```
Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

GNT's 1,2,4,5, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

#### FIG. 371

```
Yeast expressed IF-gamma.

a-m=0; q-y (independently selected) = 0 to 1; p=1;

R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

### FIG. 37J

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase.

```
a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-transferrin.
```

## FIG. 37K

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1; n, v-y = 0.
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1;
n, v-y (independently selected) = 0 or 1;
R = PEG.
```

ST3Gal3

### FIG. 37L

# 138/498

```
Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 & 2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, q (independently selected) = 0 or 1;
p = 1; v, x (independently selected) = 1,
when e, g (independently selected) is 1;
R = PEG.
```

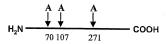
#### FIG. 37M

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-PEG, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-2;
v-y (independently selected) = 1,
when j-m (independently selected) = 2;
R = PEG.
```

#### FIG. 37N



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & \\ -\operatorname{GlcNAc-GlcNAc-Man} & & & \\ -\operatorname{GlcNAc-GlcNAc-Man} & & & \\ & & & & \\ -\operatorname{GlcNAc-GlcNAc-Man} & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & &$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 38A

CHO, BHK, 293 cells, Vero or transgenic animal expressed  $\alpha_1$  antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

 Sialidase
 CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

#### FIG. 38B

CHO, BHK, 293 cells, Vero or transgenic animal expressed  $\alpha_1$  antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

 Sialidase
 CMP-SA-PEG (1.2 mol eq), ST3Gal3
 CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG

FIG. 38C

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed alpha-1 antitrypsin.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

ST3Gal3
3. CMP-SA. ST3Gal3

#### FIG. 38D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub>-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

#### **FIG. 38E**

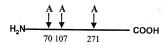
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CHO, BHK, 293 cells, Vero expressed  $\alpha_1$ -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 38F



$$\mathbf{A} \overset{(\mathrm{Fuc})_{i}}{\overset{|}{\operatorname{GleNAc\text{-}(Gal)}_{k}]_{e^{-}}(\mathrm{Sia})_{i} - (R)_{v}}}{\underset{(\mathrm{R}')_{n}}{\operatorname{GleNAc\text{-}Man}}} \underbrace{\left[ [\mathrm{GleNAc\text{-}(Gal)}_{k}]_{e^{-}}(\mathrm{Sia})_{i} - (R)_{v} \right]_{r}^{r}}_{\left[ [\mathrm{GleNAc\text{-}(Gal)}_{k}]_{e^{-}}(\mathrm{Sia})_{i} - (R)_{x} \right]_{t}} \underbrace{\left[ [\mathrm{GleNAc\text{-}(Gal)}_{k}]_{h^{-}}(\mathrm{Sia})_{m^{-}}(R)_{y} \right]_{u}}_{q_{p}} \underbrace{\left[ [\mathrm{GleNAc\text{-}(Gal)}_{k}]_{h^{-}}(\mathrm{Sia})_{m^{-}}(R)_{y} \right]_{u}}_{u}}_{u}}_{u}$$

a-d, i, n, p-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

v-y=0;

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 38G

# 144/498

```
Insect or fungi cell expressed \alpha_1-antitrypsin. a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1; j-m = 0; v-y (independently selected) = 1, when e-h (independently selected) is 1; R=PEG.
```

### FIG. 38H

```
Yeast expressed \alpha_1-antitrypsin.

a-m=0; q-y (independently selected) = 0 to 1;

p=1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- ↓ 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

#### FIG. 381

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CHO, BHK, 293 cells, Vero expressed  $\alpha_1$ -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

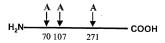
- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

a-m, q-u (independently selected) = 0 or 1: p = 1; n = 0;v-y (independently selected) = 0 or 1;

R = linker-transferrin.

FIG. 38J

## 146/498



$$(Fuc)_{i} \\ \mathbf{A} \leftarrow (Glc)_{i} \\ \mathbf{A} \leftarrow (Glc)_{i} \\ (R')_{p} \\ (R')_{q} \\ (R$$

a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer;

R', R" (independently selected) = sugar, glycoconjugate.

FIG. 38K

## 147/498

```
Yeast expressed alpha-1 antitrypsin. a-h, i-m, p, q = 0;
```

R (independently selected) = mannose, oligomannose, polymannose;

r-u, v-y (independently selected) = 0 or 1; n, o = 1.

- endoglycanase
- ▼ 2. Galactosyltransferase, UDP-Gal-PEG

```
a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.
```

### FIG. 38L

```
Plant expressed alpha-1 antitrypsin.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n=1; R'=xylose
```

- 1. hexosaminidase.
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, v-y = 0;
c, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.
```

#### FIG. 38M

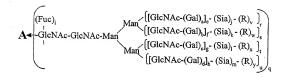
CHO, BHK, 293 cells, Vero, transgenic animal expressed  $\alpha_1$  antitrypsin. a-h, i-o, r-u (independently selected) = 0 or 1; p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 38N





a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 39A

CHO, BHK, 293 cells, Vero expressed Cerezyme a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

### FIG. 39B

```
CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
  2. CMP-SA-M-6-P (1.2 mol eq),
  ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = mannose-6-phosphate
```

#### FIG. 39C

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
    CMP-SA, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = Mannose-6-phosphate
```

#### FIG. 39D

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; y-y = 0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-spacer-M-6-P or clustered M-6-P
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = M-6-P or clustered M-6-P
```

### FIG. 39E

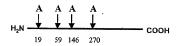
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

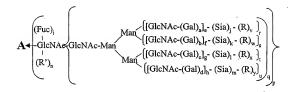
1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 39F

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a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 39G

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```
Insect cell expressed Cerezyme.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

### FIG. 39H

```
Yeast expressed Cerezyme.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
   Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG. ST3Gal3
- a-m, p-y=0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

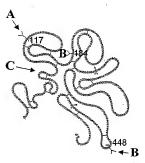
## FIG. 391

CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.3. CMP-SA, ST3Gal3
- a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-transferrin.

FIG. 39J

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$$\begin{array}{c} (Fuc)_{i} \\ \textbf{B} \leftarrow -\text{GlcNAc} - (Gal)_{a}l_{e}^{-} \cdot (Sia)_{j}^{-} \cdot (R)_{v} \\ (R')_{o} \end{array} \\ \begin{array}{c} \text{Man} \left[ [\text{GlcNAc} - (Gal)_{a}l_{e}^{-} \cdot (Sia)_{j}^{-} \cdot (R)_{v} \right]_{g}^{r} \\ \left[ (\text{GlcNAc} - (Gal)_{e}l_{g}^{-} \cdot (Sia)_{k}^{-} \cdot (R)_{x} \right]_{t}^{r} \\ \left[ (\text{GlcNAc} - (Gal)_{e}l_{g}^{-} \cdot (Sia)_{i}^{-} \cdot (R)_{y} \right]_{u} \\ \end{array}$$

$$C \longleftarrow \text{-(Fuc)}_{0-1} \qquad A \longleftarrow \text{-GlcNAc-GlcNAc-Man} \qquad \underbrace{\text{Man-[Man]}_{0-12}}_{\text{Man}}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 40A

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n=1; h=1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; o, v-y = 0.
```

```
1. Mannosidase(s), sialidase
2. GNT1,2 (4 and/or 5) UDP-GlcNAc
3. Gal transferase, UDP-Gal
4. CMP-SA-PEG, ST3Gal3
```

```
 A=B; \ a-g, \ n=1; \ h=1 \ to \ 3; \\ i, r-u \ (independently \ selected)=0 \ or \ 1; \\ o=0; \ j-m, v-y \ (independently \ selected)=0 \ or \ 1; \\ R=PEG
```

#### FIG. 40B

```
\label{eq:approx} \begin{split} &\text{Insect or fungi cell expressed tPA} \\ &A=B; \ a\text{-d}, f, h, j\text{-o}, s, u, v\text{-y}=0; \\ &e, g, i, n, r, \ t \ (independently selected)=0 \ \text{or} \ 1. \end{split}
```

```
1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG. ST3Gal3
```

```
\begin{split} A=B; & b,d,f,h,k,m,o,s,u,w,y=0;\\ a,c,e,g,i,r,t & (independently selected)=0 \text{ or } 1;\\ n=1; & j,l,v,x & (independently selected)=0 \text{ or } 1;\\ R=PEG. \end{split}
```

#### FIG. 40C

```
Yeast expressed tPA
B = A; i = 0.
```

- endoglycanase
   Galactosyltransferase,
   UDP-Gal-PEG
- A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

### FIG. 40D

$$\begin{split} &\text{Insect or fungi cell expressed tPA} \\ &A=B; \ a\text{-d}, f, h, j\text{-o}, s, u, v\text{-y}=0; \\ &e, g, i, n, r, \ t \ (independently selected)=0 \ or \ 1. \end{split}$$

- 1. alpha and beta mannosidases
- 2. Galactosyltransferase, UDP-Gal-PEG

A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

#### FIG. 40F

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```
Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
\begin{array}{lll} A=B; & b,d, \ f, \ h, \ j\text{-o}, s, u, w, y=0; \\ a,c,e,g, \ i, \ r, \ t, v, \ x \ (independently \ selected)=0 \ or \ 1; \\ n=1; \ R=PEG. \end{array}
```

#### FIG. 40F

```
Insect or fungi cell expressed tPA A=B;\ a-d,\ f,\ h,\ j-o,\ s,\ u,\ v-y=0; e, g, i, n, r, t (independently selected) = 0 or 1.
```

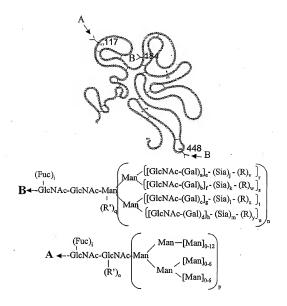
- GNT's 1 & 2, UDP-GlcNAc
   Galactosidase (synthetic enzyme),
- 2. Galactosidase (synthetic enzyme)

  ▼ PEG-Gal-F.

A = B; b, d, f, h, j-o, s, u, w, y = 0; a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1; n = 1; R = PEG.

## FIG. 40G

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a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 40H

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```
NSO expressed tPA

A = B; a-m, r-u (independently selected) = 0 or 1;

n = 1; o, p, q, v-y = 0
```

sialidase, alpha-galactosidase
 CMP-SA-levulinate, ST3Gal3,
 H<sub>4</sub>N<sub>2</sub>-PEG

```
 A = B; \ a\text{-m, r-y (independently selected)} = 0 \ \text{or} \ 1; \\ n = 1; \ o, p, q = 0; \\ v\text{-y (independently selected)} = 1, \\ \text{when j-m (independently selected)} \ is \ 1; \\ R = PEG.
```

#### FIG. 401

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n, p = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; q, o, v-y = 0.
```

- 1. alpha and beta Mannosidases
- 2. CMP-SA, ST3Gal3
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1; o = 1;
q, p, v-y = 0; j-m (independently selected) = 0 or 1;
R' = Gal - PEG
```

### FIG. 40J

#### Plant expressed tPA

A = B; a-d, f, h, j-m, s, u, v-y = 0;

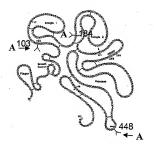
e, g, i, q, r, t (independently selected) = 0 or 1; n=1; R' = xylose

- 1. hexosaminidase,
- 2. alpha mannosidase and
  - xylosidase

3. GlcNAc transferase, UDP-GlcNAc-PEG

A = B; a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0; q = 1; R' = GlcNAc-PEG.

FIG. 40K



$$\mathbf{A} = \underbrace{\left[ [\operatorname{GlcNAc-(Gal)}_a]_e^- \left( \operatorname{Sia} \right)_j^- \left( \operatorname{R} \right)_v \right]_r}_{\left[ [\operatorname{GlcNAc-(Gal)}_b]_f^- \left( \operatorname{Sia} \right)_k^- \left( \operatorname{R} \right)_w \right]_s}_{\left[ [\operatorname{GlcNAc-(Gal)}_b]_g^- \left( \operatorname{Sia} \right)_i^- \left( \operatorname{R} \right)_x \right]_t}_{\left[ [\operatorname{GlcNAc-(Gal)}_d]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u} \underbrace{\left[ \left( \operatorname{GlcNAc-(Gal)}_b \right)_g^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left( \operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left(\operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_y \right]_u}_{\left[ \operatorname{GlcNAc-(Gal)}_d \right]_h^- \left(\operatorname{Sia} \right)_m^- \left( \operatorname{R} \right)_u}_{\left[ \operatorname{ClcNAc-(Gal)}_h^- \left( \operatorname{ClcNAc-(G$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 40L

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CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

### FIG. 40M

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
  2. CMP-SA-PEG (1.2 mol eq),
  ST3Gal3
  - 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

#### **FIG. 40N**

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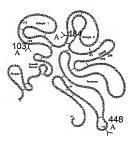
```
NSO expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0; Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and  $\alpha$ -galactosidase 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 400

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$$\mathbf{A} \leftarrow \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_a}]_e \cdot (\operatorname{Sia})_j \cdot (R)_v \\ [\operatorname{GlcNAc-GlcNAc-Man}]_t \\ [\operatorname{GlcNAc-(Gal)_b}]_t \cdot (\operatorname{Sia})_k \cdot (R)_w \end{bmatrix}_t \\ [\operatorname{GlcNAc-(Gal)_b}]_t \cdot (\operatorname{Sia})_t \cdot (R)_v \end{bmatrix}_t \cdot \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_a}]_e \cdot (\operatorname{Sia})_t \cdot (R)_v \\ [\operatorname{GlcNAc-(Gal)_a}]_h \cdot (\operatorname{Sia})_m \cdot (R)_y \end{bmatrix}_u \end{bmatrix}_t \cdot \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_m \cdot (R)_y \\ [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_m \cdot (R)_y \end{bmatrix}_u \end{bmatrix}_t \cdot \begin{bmatrix} \operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \\ [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_m \cdot (R)_y \end{bmatrix}_u \end{bmatrix}_t \cdot \begin{bmatrix} \operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_v \\ [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \end{bmatrix}_u \cdot \begin{bmatrix} \operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \\ [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \end{bmatrix}_u \cdot \begin{bmatrix} \operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \\ [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \end{bmatrix}_u \cdot \begin{bmatrix} \operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \\ [\operatorname{GlcNAc-(Gal)_a}]_t \cdot (\operatorname{Sia})_t \cdot (R)_y \end{bmatrix}_u \cdot (R)_y \cdot (R$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
  - CMP-SA-PEG (16 mol eq), ST3Gal3
  - 3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

### FIG. 40Q

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- CMP-SA-levulinate, ST3Gal3, buffer, salt
   H<sub>4</sub>N<sub>7</sub>-PEG
- a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1;

R = PEG.

#### FIG. 40R

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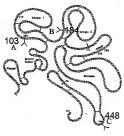
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 40S

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & (\operatorname{R"})_{0} & (\operatorname{Gal})_{a}]_{e}^{-} (\operatorname{Sia})_{i}^{-} (\operatorname{R})_{v} \end{bmatrix}_{i} \\ \operatorname{GlcNAc-Gal}_{i} & \operatorname{GlcNAc-Man}_{i} & (\operatorname{GlcNAc-Gal})_{a}]_{e}^{-} (\operatorname{Sia})_{e}^{-} (\operatorname{R})_{v} \end{bmatrix}_{i} \\ \operatorname{GlcNAc-Gal}_{i} & \operatorname{Man}_{i} & (\operatorname{GlcNAc-Gal})_{d}]_{h}^{-} (\operatorname{Sia})_{i}^{-} (\operatorname{R})_{v} \end{bmatrix}_{u} \\ \operatorname{GlcNAc-Gal}_{i} & \operatorname{Man}_{i} & (\operatorname{GlcNAc-Gal})_{d}]_{h}^{-} (\operatorname{Sia})_{i}^{-} (\operatorname{R})_{v} \end{bmatrix}_{u} \\ \operatorname{GlcNAc-Gal}_{i} & \operatorname{Gal}_{i} & \operatorname{$$

a-d, i, n-y (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

R" = glycosyl residue.

FIG. 40T

```
Insect cell expressed TNK tPA
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

GNT's 1,2,4,5, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

#### FIG. 40U

```
Yeast expressed TNK tPA a-m=0; q-y (independently selected) = 0 to 1; p=1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
   Galactosyltransferase, UDP-Gal-PEG
- a-m, p-y = 0; n (independently selected) = 0 or 1; R' =-Gal-PEG.

#### **FIG. 40V**

# 171/498

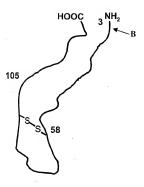
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

```
1. CMP-SA-linker-Gal-UDP,
ST3Gal3
```

2. Galactosyltransferase, anti-TNF IG chimera produced in CHO.

a-m, r-u (independently selected) = 0 or 1; p, q = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-anti-TNF IG chimera protein.

FIG. 40W



$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc} - (\mathrm{Gal})_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligomannose.

FIG. 41A

# 173/498

CHO, BHK, 293 cells, Vero expressed IL-2 a-c, e (independently selected) = 0 or 1; d = 0

1. Sialidase 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

# FIG. 41B

Insect cell expressed IL-2 a, e (independently selected) = 0 or 1; b, c, d = 0.

Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 41C

```
E. coli expressed IL-2
a-e = 0.

1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
```

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

## FIG. 41D

```
NSO expressed IL-2
a, e (independently selected) = 0 or 1;
b, c, d = 0

1. CMP-SA-levulinate, ST3Gal1
2. H_4N_2-PEG

a, c, d, e (independently selected) = 0 or 1;
```

FIG. 41F

b = 0; R = PEG.

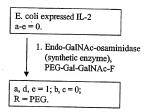


FIG. 41F

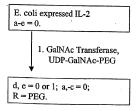


FIG. 41G

2 peptides
A and A' - N-linked sites
B - O-linked sites

a-d, i, n-u (independently selected) = 0 or 1.

aa, bb (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

v-z = 0; R = polymer, glycoconjugate.

FIG. 42A

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```
CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed
Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;
v-z = 0.
```

1. Sialidase
2. CMP-SA-PEG, ST3Gal3

```
e-h = 1 to 4;
aa, bb, a-d, i, n, q-u (independently selected) = 0 or 1;
o, p, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

#### FIG. 42B

```
CHO, BHK, 293S cells, Vero, MDCK, 293S, HEKC expressed Factor VIII. e-h = 1 to 4; aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1; v-z = 0.
```

```
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
3. ST3Gal1, CMP-SA
```

```
e-h = 1 to 4;
aa, bb, a-d, i, n, p-u (independently selected) = 0 or 1;
o, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

#### FIG. 42C

## 178/498

```
CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.
```

# 1. CMP-SA-PEG, ST3Gal3

```
e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

#### FIG. 42D

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) 0 or 1;
v-z = 0.
```

### 1. CMP-SA-PEG, ST3Gal1

```
e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

#### FIG. 42E

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.

### 1. CMP-SA-PEG, $\alpha$ 2,8-ST

e-h = 1 to 4; aa, bb, a-d, i, n-y (independently selected) = 0 or 1; z = 0; j-m (independently selected) = 0 to 2; v-y (independently selected) = 1, when j-m (independently selected) is 2; R = PEG.

# FIG. 42F

## 180/498

2 peptides

A or A' - N-linked sites

B - O-linked sites

$$A = (\operatorname{Fuc})_{i} \setminus (\operatorname{Fuc})_{i} \setminus (\operatorname{GicNAc-(Gal)_al_e^-}(\operatorname{Sia})_{i}^- (\operatorname{R})_{v}) \setminus (\operatorname{GicNAc-(Gal)_al_e^-}(\operatorname{Sia})_{i}^- (\operatorname{R})_{v}) \setminus (\operatorname{GicNAc-(Gal)_al_e^-}(\operatorname{Sia})_{i}^- (\operatorname{R})_{v}) \setminus (\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{Sia})_{i}^- (\operatorname{R})_{v}) \setminus (\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{Sia})_{m}^- (\operatorname{R})_{v}) \setminus (\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_al_a^-}(\operatorname{GicNAc-(Gal)_a^-}(\operatorname{GicNAc-(Gal)_a^-}(\operatorname{GicNAc-(Gal)_a^-}(\operatorname{GicNAc-(Gal)_a^-}(\operatorname{GicNAc-(Gal)_a^-}(\operatorname{GicNAc-(G$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc} - (\operatorname{Gal})_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{bmatrix}_{q}$$

glycoconjugate.

$$A^{2} \longleftarrow (Fuc)_{i} \qquad (Man)_{0.2} \qquad (R')_{ad} \qquad (Man)_{0.2} \qquad (Man)_{0.2$$

a-d, i, n-u, (independently selected) = 0 or 1.

aa, bb, cc, dd (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

v-z = 0;

R = modifying group, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group,

FIG. 42G

## 181/498

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

1. CMP-SA-levulinate, ST3Gal3, 2. H<sub>4</sub>N<sub>2</sub>-PEG

```
e-h = 1 to 4; aa, bb, cc, a-d, i, n-u (independently selected) = 0 or 1; dd, z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.
```

### FIG. 42H

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII. c-h=1 to 4; aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1; dd, v-z=0.
```

```
    1. endo-H
    2. galactosyltransferase, UDP-Gal-PEG
```

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

#### FIG. 421

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC
expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

1. ST3Gal3, CMP-SA
2. endo-H
3. galactosyltransferase, UDP-Gal-PEG
```

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
```

cc, v-z=0: R'=-Gal-PEG.

#### FIG. 42J

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

```
1. mannosidases
2. GNT 1 & 2, UDP-GlcNAc
3. galactosyltransferase, UDP-Gal-PEG
```

```
e-h = 1 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0; R = PEG.
```

#### FIG. 42K

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII. e-h = 1 to 4; aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1; dd, v-z = 0.
```

- 1. mannosidases
- 2. GNT-1,2, 4 & 5; UDP-GlcNAc
- ▼ 3. galactosyltransferase, UDP-Gal
   4. ST3Gal3, CMP-SA

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, j-q (independently selected) = 0 or 1;
dd, v-z=0.
```

#### FIG. 42L

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII. e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1; dd, v-z = 0.
```

```
    1. mannosidases
    ▼ 2. GNT-1, UDP-GlcNAc-PEG
```

```
e-h=0 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z=0.
```

#### FIG 42M



$$\mathbf{A} \leftarrow \begin{bmatrix} [\operatorname{GlcNAc-(Gal)}_a]_e^- & (\operatorname{Sia})_j - (R)_v \\ -\operatorname{GlcNAc-GlcNAc-Man} \end{bmatrix}_t^r \\ \begin{bmatrix} [\operatorname{GlcNAc-(Gal)}_b]_l^- - (\operatorname{Sia})_k - (R)_v \\ -\operatorname{GlcNAc-(Gal)}_b]_l^- & (\operatorname{Sia})_l - (R)_x \\ -\operatorname{Man} \begin{bmatrix} [\operatorname{GlcNAc-(Gal)}_a]_g^- & (\operatorname{Sia})_l - (R)_x \\ -\operatorname{GlcNAc-(Gal)}_a]_l^- & (\operatorname{Sia})_m^- & (R)_y \\ -\operatorname{GlcNAc-(Gal)}_a & (\operatorname{Sia})_m^- & (R)_y \\ -\operatorname{GlcNAc-(Gal)}_a & (\operatorname{Sia})_m^- & (R)_y \\ -\operatorname{GlcNAc-(Gal)}_a & (R)_y \\ -\operatorname{GlcNAc-(Gal)}_$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 43A

# 185/498

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

```
1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

#### FIG. 43B

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

```
1. Sialidase
2. CMP-SA-PEG (1.2 mol eq),
ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3
```

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

#### FIG. 43C

## 186/498

```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG
```

### FIG. 43D

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3,
buffer, salt
2. H<sub>4</sub>N<sub>2</sub>-PEG

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

CHO, BHK, 293 cells, Vero expressed Urokinase.

#### FIG. 43E

## 187/498

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 43F



$$\mathbf{A} \leftarrow \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_a]_c^-}(\operatorname{Sia})_j^- (R)_v \end{bmatrix}^T_{[\operatorname{GlcNAc-Man}} \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_a]_c^-}(\operatorname{Sia})_j^- (R)_w \end{bmatrix}^T_{[\operatorname{GlcNAc-(Gal)_a]_c^-}(\operatorname{Sia})_j^- (R)_x \end{bmatrix}^T_{[\operatorname{GlcNAc-(Gal)_a]_c^-}(\operatorname{Sia})_j^- (R)_x \end{bmatrix}^T_{[\operatorname{GlcNAc-(Gal)_a]_c^-}(\operatorname{Sia})_j^- (R)_y \end{bmatrix}_{q}^T_{q}$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 43G

## 189/498

```
Insect cell expressed Urokinase.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-n = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

#### FIG. 43H

```
Yeast expressed Urokinase.
a-n = 0;
q-y (independently selected) = 0 to 1;
p = 1; R (branched or linear) = Man, oligomannose.
```

```
    Endoglycanase
    Galactosyltransferase, UDP-Gal
    CMP-SA-PEG, ST3Gal3
```

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

#### FIG. 431

# 190/498

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.
```

```
    CMP-SA-linker-SA-CMP, ST3Gal3
    ST3Gal1, desialylated Urokinase produced in CHO.
    3. CMP-SA, ST3Gal3, ST3Gal1
```

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-Urokinase.
```

#### FIG. 43J

```
Isolated Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0; n = 0; Sia (independently selected) = Sia or SO_4; Gal (independently selected) = Gal or GalNAc; GleNAc (independently selected) = GleNAc or GleNAc-Fuc.
```

1. sulfohydrolase

```
a-d, i-m, q-u (independently selected) = 0 or 1;
n = 0; e-h = 1; Sia = Sia;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
v-y (independently selected) = 0 or 1;
R = PEG
```

2. CMP-SA-PEG, sialyltransferase

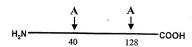
### FIG. 43K

Isolated Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; n = 0; v-y = 0; Sia (independently selected) = Sia or  $SO_4$ ; Gal (independently selected) = Gal or GalNAc; GleNAc (independently selected) = GleNAc or GleNAc-Fuc,

- 1. sulfohydrolase, hexosaminidase
- 2. UDP-Gal-PEG, galactosyltransferase

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-n = 0; Gal (independently selected) = Gal; GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 43L



$$\mathbf{A} = \begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{a}]_{e}^{-} \cdot (\mathrm{Sia})_{j}^{-} \cdot (\mathrm{R})_{v} \end{bmatrix}_{t}^{t}$$

$$\begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{b}]_{r}^{-} \cdot (\mathrm{Sia})_{k}^{-} \cdot (\mathrm{R})_{w} \end{bmatrix}_{t}^{t}$$

$$\begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{d}]_{e}^{-} \cdot (\mathrm{Sia})_{l}^{-} \cdot (\mathrm{R})_{x} \end{bmatrix}_{t}^{t}$$

$$\begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{d}]_{h}^{-} \cdot (\mathrm{Sia})_{m}^{-} \cdot (\mathrm{R})_{y} \end{bmatrix}_{u}^{t}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 44A

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.
```

1. Sialidase
2. CMP-SA-PEG (16 mol eq),

ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

### FIG. 44B

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

1. Sialidase 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

## FIG. 44C

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq), ST3Gal3
    CMP-SA, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

# FIG. 44D

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

### FIG. 44E

# 195/498

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

### 1. CMP-SA, α2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

### FIG. 44F

## 196/498



$$\begin{array}{c} \textbf{A} & \overbrace{(\text{Fuc})_{i}}^{\text{(Fuc)}_{i}} & \overbrace{(\text{GlcNAc-(Gal)}_{a}]_{e^{-}}(\text{Sia})_{i}^{-}(R)_{v}}^{\text{(Fuc)}_{i}} \\ & \overbrace{(\text{GlcNAc-(Gal)}_{b}]_{r^{-}}(\text{Sia})_{k^{-}}(R)_{w}}^{\text{(IGlcNAc-(Gal)}_{b}]_{r^{-}}(\text{Sia})_{r^{-}}(R)_{x}}^{\text{(IGlcNAc-(Gal)}_{d}]_{b^{-}}(\text{Sia})_{r^{-}}(R)_{y}} \\ & \underbrace{(\text{IGlcNAc-(Gal)}_{d}]_{b^{-}}(\text{Sia})_{r^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d}]_{b^{-}}(\text{Sia})_{r^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d}]_{b^{-}}(R)_{y}} \\ & \underbrace{(\text{IGlcNAc-(Gal)}_{d}]_{b^{-}}(\text{Sia})_{r^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}} \\ & \underbrace{(\text{IGlcNAc-(Gal)}_{d})_{b^{-}}(\text{Sia})_{r^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}} \\ & \underbrace{(\text{IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}} \\ & \underbrace{(\text{IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}} \\ & \underbrace{(\text{IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{y}}^{\text{(IGlcNAc-(Gal)}_{d})_{b^{-}}(R)_{$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 44G

```
Insect cell expressed DNase I. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1; j-n = 0; v-y (independently selected) = 1, when e-h (independently selected) is 1; R = PEG. \label{eq:period}
```

### FIG. 44H

```
Yeast expressed DNase I.
a-n = 0;
q-y (independently selected) = 0 to 1;
p = 1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
   Galactosyltransferase, UDP-Gal
- ↓ 3. CMP-SA-PEG, ST3Gal3

```
a-n, p-y=0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

#### FIG. 441

## 198/498

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- ST3Gal1, desialylated alpha-1-Proteinase inhibitor.
  - 3. CMP-SA, ST3Gal3, ST3Gal1

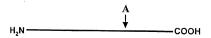
a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker- alpha-1-Proteinase inhibitor.

FIG. 44J

### 199/498



$$\begin{array}{c} (\operatorname{Fuc})_{i} \\ \mathbf{A} \longleftarrow (\operatorname{GlcNAc-Man})_{i} \\ (R')_{n} \end{array} \\ \begin{array}{c} (\operatorname{GlcNAc-(Gal)}_{a,l_{c}} - (\operatorname{Sia})_{j} - (R)_{v})_{r} \\ (\operatorname{GlcNAc-Man})_{s} \\ (\operatorname{GlcNAc-(Gal)}_{a,l_{c}} - (\operatorname{Sia})_{s} - (R)_{w})_{s} \\ (\operatorname{GlcNAc-(Gal)}_{a,l_{c}} - (\operatorname{Sia})_{i} - (R)_{x})_{t} \\ (\operatorname{GlcNAc-(Gal)}_{a,l_{c}} - (\operatorname{Sia})_{m} - (R)_{y})_{u} \\ \end{array}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 45A

# 200/498

```
CHO, BHK, 293 cells, Vero expressed Insulin. a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.
```

```
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
```

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

### FIG. 45B

Insect cell expressed Insulin.

```
a-h, j-n, s-y = 0;

i, r (independently selected) = 0 or 1; z = 1.

1. GNT's 1&2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;

e, g, i, r, t, v, x (independently selected) = 0 or 1;

v, x (independently selected) = 1,

when e, g (independently selected) is 1;

z = 1; R = PEG.
```

#### FIG. 45C

# 201/498

Yeast expressed Insulin.

a-n=0; r-y (independently selected) = 0 to 1;

z = 1;

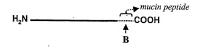
R (branched or linear) = Man, oligomannose or polysaccharide.

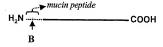
1. Endo-H

2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 45D





$$\mathbf{B} \quad \overset{\text{(Sia)}_{b}}{\leftarrow} \quad \overset{\text{(Sia)}_{c}}{\operatorname{GalNAc-(Gal)}_{a}\text{-(Sia)}_{c}\text{- (R)}_{d}}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 45E

# 203/498

CHO, BHK, 293 cells, Vero expressed insulinmucin fusion protein.

- a-c, e (independently selected) = 0 or 1; d = 0
  - 1. Sialidase
  - 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

### FIG. 45F

Insect cell expressed Insulin-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 45G

E. coli expressed Insulin-mucin fusion protein. a-e=0.

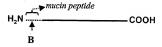
GalNAc Transferase, UDP-GalNAc
 CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 45H

### 205/498





$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{b} \\ -(\operatorname{GalNAc-(Gal)}_{a}-(\operatorname{Sia})_{c}-(R)_{d} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligo-mannose.

FIG. 451

# 206/498

E. coli expressed Insulin-mucin fusion protein. a-e, n=0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

## FIG. 45J

E. coli expressed Insulin-mucin fusion protein. a-e, n = 0.

- GalNAc Transferase,
   UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

#### FIG. 45K

E. coli expressed Insulin (N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e = 0; n = 1; R' = linker-transferrin.

FIG. 45L

$$(Acyl)_{0-1}HN \xrightarrow{4} \xrightarrow{4} \xrightarrow{146} COOH$$

$$A \qquad A$$

$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i & \operatorname{Man} \left( [\operatorname{GlcNAc-(Gal)_a}]_e \cdot (\operatorname{Sia})_i - (R)_v \right)_s^T \\ -\operatorname{GlcNAc-GlcNAc-Man} & \operatorname{Man} \left( [\operatorname{GlcNAc-(Gal)_b}]_e \cdot (\operatorname{Sia})_k - (R)_w \right)_s^T \\ \operatorname{Man} \left( [\operatorname{GlcNAc-(Gal)_c}]_g \cdot (\operatorname{Sia})_i - (R)_x \right)_t \\ \left( [\operatorname{GlcNAc-(Gal)_d}]_h \cdot (\operatorname{Sia})_m \cdot (R)_y \right)_u \\ -\operatorname{GalNAc-(Gal)_n^-(Sia)_p^-}(R)_z \end{bmatrix}_{aa} \end{bmatrix}$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 46A

## 209/498

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.

 Sialidase
 CMP-SA-linker-lipid-A, ST3Gal3

a-d, i-m, q-u, aa (independently selected) = 0 or 1; o, p, z = 0; n, e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = linker-lipid-A.

### FIG. 46B

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.

- sialidase
   CMP-SA-linker-tetanus toxin, ST3Gal1

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1; o, v-y = 0; n, e-h = 1; R = tetanus toxin.

### FIG. 46C

```
NSO expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

```
    α-galactosidase
    CMP-SA, ST3Gal3
    CMP-SA-KLH, ST3Gal1
```

```
a-d, i-n, p-u, z, aa (independently selected) = 0 or 1;
e-h = 1; o, v-y = 0;
z = 1, when p = 1;
R = KLH.
```

#### FIG. 46D

```
Yeast expressed M-antigen.
a-p, z = 0; q-y, aa (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

```
    α1,2-mannosidase
    GNT 1,
    UDP-GlcNAc-linker-diphtheria toxin.
```

```
e, q, l, m, r, t, u, v, aa (independently selected) =0 or 1;
a-d, f-h, j, k, n-p, s, w-z = 0;
Sia = Man; R = linker-diphtheria toxin.
```

### FIG. 46E

## 211/498

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

CMP-SA-levulinate, ST3Gal3,
 H<sub>4</sub>N<sub>2</sub>-linker-DNA

a-d, i-m, o-y, aa (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = linker-DNA.

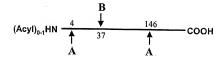
### FIG. 46F

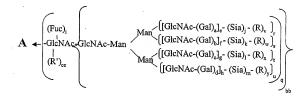
CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-n, o-u, aa (independently selected) = 0 or 1; e-h = 1; v-z = 0.

1. CMP-SA, poly-α2,8-ST

a-d, i, n-u, aa (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-100; v-z (independently selected) = 0.

FIG. 46G





$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GaINAc-(GaI)}_{n} - (\operatorname{Sia})_{p} - (\operatorname{R})_{z} \end{bmatrix}_{aa}$$

a-d, i, n, q-u, aa, bb, (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-p (independently selected) = 0 to 100. Cc, v-y = 0; R = modifying group, mannose, oligo-mannose. R'=H, glycosyl residue, modifying group, glycoconiugate.

FIG. 46H

# 213/498

```
Insect cell expressed M-antigen.
a-d, f, h, j-m, o, p, s, u, v-z, cc = 0;
bb = 1;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

 GNT-2, UDP-GlcNAc-linker-Neisseria protein

```
\label{eq:continuous} \begin{split} &a,c,e,g,i,n,q,r,t,v,x, aa~(independently~selected) = \\ &0~or~1;\\ &b,d,f,h,j\text{-}p,s,u,w,y,z,cc=0;\\ &bb=1;~R=\text{-}linker\text{-}Neisseria~protein.} \end{split}
```

#### FIG. 461

```
Yeast expressed M-antigen.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

- Endoglycanase
   Galactosyltransferase,
   UDP-Gal-linker-Neisseria protein
- ▼ UDP-Gal-linker-Neisseria proteir

```
a-p, r-z, bb = 0;
q, aa, cc (independently selected) = 0 or 1;
R' = -Gal-linker-Neisseria protein.
```

FIG. 46J

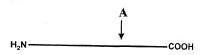
#### Yeast expressed M-antigen.

- a-p, z, cc = 0;
- q-y, aa (independently selected) = 0 to 1; bb = 1;
- R (branched or linear) = Man, oligomannose;
- GalNAc = Man.
  - 1. mannosidases

  - 2. GNT 1 & 2, UDP-GlcNAc
    3. UDP-Gal, Galactosyltransferase,
- a, c, e, g, j, l, q, r, t, aa (independently selected) = 0 or 1;
- b, d, f, h, k, m-p, s, u-z, cc = 0; bb = 1.

### FIG. 46K

## 215/498



$$\begin{array}{c} (\operatorname{Fuc})_{i} \\ \mathbf{A} \leftarrow \operatorname{GlcNAc} - \operatorname{GlcNAc} - \operatorname{GlcNAc} - \operatorname{Man} \\ (R')_{n} \end{array} \\ \begin{bmatrix} \operatorname{GlcNAc} - (\operatorname{Gal})_{a} \right]_{e}^{-} \cdot (\operatorname{Sia})_{j}^{-} \cdot (R)_{v} \\ \left[ \left[ \operatorname{GlcNAc} - (\operatorname{Gal})_{e} \right]_{f}^{-} \cdot (\operatorname{Sia})_{k}^{-} \cdot (R)_{w} \right]_{t}^{t} \\ \left[ \left[ \operatorname{GlcNAc} - (\operatorname{Gal})_{e} \right]_{g}^{-} \cdot (\operatorname{Sia})_{l}^{-} \cdot (R)_{y} \right]_{u} \\ \end{bmatrix}_{u} \end{array}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconiugate.

FIG. 47A

### 216/498

CHO, BHK, 293 cells, Vero expressed Growth Hormone.

a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

a-m, r-u (independently selected) = 0 or 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; n = 0; R = PEG; z = 1.

#### FIG. 47B

Insect cell expressed growth hormone. a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1; z = 1.

1. GNT's 1&2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0; e, g, i, r, t, v, x (independently selected)= 0 or 1; v, x (independently selected) = 1, when e, g (independently selected) is 1; z = 1; R = PEG.

#### FIG. 47C

Yeast expressed growth hormone.

a-n = 0; r-y (independently selected) = 0 to 1;

z = 1;

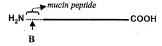
R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 47D





$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0;

R = modifying group, mannose, oligomannose.

FIG. 47E

CHO, BHK, 293 cells, Vero expressed growth hormone-mucin fusion protein.

a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

#### FIG. 47F

Insect cell expressed Growth Hormone-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 47G

E. coli expressed growth hormone-mucin fusion protein. a-e=0.

GalNAc Transferase, UDP-GalNAc
 CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

# FIG. 47H

E. coli expressed growth hormone-mucin fusion protein.

a-e, n = 0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

#### FIG. 471

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E. coli expressed growth hormone-mucin fusion protein.

a-e, n = 0.

- GalNAc Transferase,
   UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin

  ▼ 3. CMP-SA. ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

### FIG. 47J

E. coli expressed growth hormone (N)—no mucin peptide.

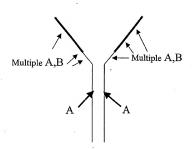
a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- ST3Gal3, asialo-transferrin
   CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

FIG. 47K

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a-d, i-m, q-u, w, z, nn, ww, zz (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4.

n, v-y = 0;

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 48A

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n=1; v-z=0.

- 1. CMP-SA, ST3Gal1
- 2. galactosyltransferase, UPD-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

#### FIG. 48B

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

1. sialidase ▼ 2. CMP-SA-PEG, ST3Gal1

a-i, p-u, z, as (independently selected) = 0 or 1; n = 1; o, j-m, v-y = 0; R = PEG.

### FIG. 48C

# 224/498

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

l. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, aa (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

#### FIG. 48D

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v = z = 0.

1. CMP-SA, ST3Gal1
2. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

#### **FIG. 48F**

```
CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
```

```
1. CMP-SA-levulinate, ST3Gal1 ··· 2. H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.
```

#### FIG. 48F

```
CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.
```

1. CMP-SA-PEG, α2,8-ST

```
a-i, o, q-u, v-z, as (independently selected) = 0 or 1; 

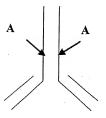
n = 1; j-m, p (independently selected) = 0 to 2; 

v-z (independently selected) = 1, 

when j-m, p (independently selected) is 2; 

R = PEG.
```

#### FIG. 48G



$$\begin{array}{c} \textbf{A} \leftarrow \begin{array}{c} \text{(Fuc)}_{i} \\ \text{GlcNAc-Man} \\ \text{(R')}_{n} \end{array} \\ \text{Man} \begin{array}{c} \left[ [\text{GlcNAc-(Gal)}_{a}]_{e^{-}} (\text{Sia})_{j^{-}} (R)_{v} \right]_{r}^{r} \\ \left[ [\text{GlcNAc-(Gal)}_{b}]_{r^{-}} (\text{Sia})_{r^{-}} (R)_{w} \right]_{s}^{r} \\ \left[ [\text{GlcNAc-(Gal)}_{d}]_{e^{-}} (\text{Sia})_{l^{-}} (R)_{y} \right]_{v^{-}} \\ \left[ [\text{GlcNAc-(Gal)}_{d}]_{h^{-}} (\text{Sia})_{m^{-}} (R)_{y} \right]_{v^{-}} \end{array}$$

a-d, i, l, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-k (independently selected) = 0 or 1.

M = 0 to 20.

n, v-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

## 227/498

CHO, BHK, 293 cells, Vero expressed Herceptin. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

```
1. galactosyltransferase, UPD-Gal
2. CMP-SA-toxin, ST3Gal3
```

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; R = toxin;
f, h, k, m, n, s, u-y=0; q, z=1;
v-y (independently selected) = 51,
when j, l (independently selected) is 1.
```

#### FIG. 49B

```
CHO, BHK, 293 cells, Vero or fungal expressed Herceptin. 
a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u - y = 0; g, z = 1.
```

 galactosyltransferase, UPD-Gal-Toxin

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

#### FIG. 49C

#### Fungi expressed Herceptin.

e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

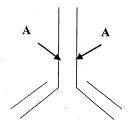
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal

a-m, r-z=0; q, n=1;

R' = -Gal-Sia-radioisotope complex.

FIG. 49D

# 229/498



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i & & & & & & & & \\ (\operatorname{GlcNAc-Man} & & & & & & \\ (\operatorname{R'})_n & & & & & & & \\ (\operatorname{GlcNAc-Man} & & & & & & \\ (\operatorname{GlcNAc-Man} & & & & & & \\ (\operatorname{GlcNAc-Gal})_p & & & & & & \\ (\operatorname{GlcNAc-Gal})_p & & & & & & \\ (\operatorname{GlcNAc-Gal})_d \end{bmatrix}_{l_n} \cdot (\operatorname{Sia})_{l_n} \cdot (\operatorname{R})_{v_j} \end{bmatrix}_{t_j}$$

a-d, i, p-u, (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 50A

# 230/498

```
CHO, BHK, 293 cells, Vero expressed Synagis.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1;
b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

2. CMP-SA-PEG, ST3Gal3

```
\begin{aligned} &a,c,i,j,w, (independently selected) = 0 \text{ or } 1;\\ &e,g,r,t=1;\ f,h,k,m,n,s,u-y=0;\\ &q,z=1;\ v-y (independently selected) = 1,\\ &when j,l (independently selected) \text{ is } 1;\\ &R=PEG. \end{aligned}
```

### FIG. 50B

```
CHO, BHK, 293 cells, Vero or fungal expressed Synagis.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

galactosyltransferase,
 UPD-Gal-PEG

```
a, c, i, w (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

#### FIG. 50C

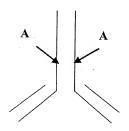
Fungi expressed Synagis. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- Galactosyltransferase, UDP-Gal
   CMP-SA-PEG, ST3Gal3

a-m, r-z=0; q, n=1; R'=-Gal-Sia-PEG.

FIG. 50D

# 232/498



$$A \leftarrow \overbrace{ \begin{bmatrix} (\operatorname{Fuc})_i \\ \operatorname{GlcNAc-Gal})_* \end{bmatrix}_s^* \cdot (\operatorname{Sia})_j - (\operatorname{R})_v \\ - \left[ (\operatorname{GlcNAc-(Gal)})_* \right]_r^* \cdot (\operatorname{Sia})_k - (\operatorname{R})_v \\ - \left[ (\operatorname{GlcNAc-(Gal)})_* \right]_r^* \cdot (\operatorname{Sia})_k - (\operatorname{R})_v \\ - \left[ (\operatorname{GlcNAc-(Gal)})_* \right]_r^* \cdot (\operatorname{Sia})_k - (\operatorname{R})_v \\ - \left[ (\operatorname{GlcNAc-(Gal)})_* \right]_r^* \cdot (\operatorname{Sia})_k - (\operatorname{Sia})_k - (\operatorname{R})_v \\ - \left[ (\operatorname{GlcNAc-(Gal)})_* \right]_r^* \cdot (\operatorname{Sia})_k - (\operatorname{$$

a-d, i, q-u, w (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51A

```
CHO, BHK, 293 cells, Vero expressed Remicade. a, c, i (independently selected) = 0 or 1; e, g, r, t=1; b, d, f, h, j-m, n, s, u-y=0; q, z=1.
```

galactosyltransferase, UPD-Gal
 CMP-SA-PEG, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1; e, g, r, t = l; f, h, k, m, n, s, u-y = 0; q, z = 1; v-y (independently selected) = l, when j, l (independently selected) is 1; R = PEG.
```

### FIG. 51B

```
CHO, BHK, 293 cells, Vero or fungal expressed Remicade. a, c, i (independently selected) = 0 or 1; e, g, t, t = 1; b, d, f, h, j-m, n_x s, u-y = 0; q, z = 1.
```

 galactosyltransferase, UPD-Gal-PEG

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1, when a, c (independently selected) is 1;
R = PEG.
```

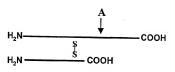
#### FIG. 51C

Fungi expressed Remicade. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3.. CMP-SA-radioisotope complex, ST3Gal3

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.
```

FIG. 51D



$$A \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i \\ \operatorname{GlcNAc-Man} \\ (\operatorname{R'})_n \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{a})_{a^-} (\operatorname{Sia})_{j^-} (R)_{v} \\ (\operatorname{GlcNAc-(Gal)}_{a})_{l^-} (\operatorname{Sia})_{k^-} (R)_{w} \end{bmatrix}_{s} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{x} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{y} \end{bmatrix}_{u} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{y} \end{bmatrix}_{u}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (\operatorname{Sia})_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{z} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{t} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{t} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{t} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{l^-} (R)_{w} \\ (\operatorname{GlcNAc-(Gal)}_{l^-})_{l^-} (R)_{w} \end{bmatrix}_{t}}_{t} \\ = \underbrace{\begin{bmatrix} (\operatorname{GlcNAc-($$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 52A

# 236/498

```
CHO, BHK, 293 cells, Vero expressed Reopro. a-m, r-u (independently selected) = 0 or 1; n=0;\ v-y=0;\ z=1.
```

```
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
```

```
a-m, r-u (independently selected) = 0 or 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; n=0; R=PEG; z=1.
```

#### FIG. 52B

```
Insect cell expressed Reopro.

a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1;

z = 1.

1. GNT's 1&2, UDP-GlcNAc-PEG
```

```
a-d, f, h, j-n, s, u, w, y=0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z=1; R=PEG.
```

#### FIG. 52C

## 237/498

```
Yeast expressed Reopro.
```

a-n = 0; r-y (independently selected) = 0 to 1; z = 1;

R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 52D



$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{pmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 52E

CHO, BHK, 293 cells, Vero expressed Reopro-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d=0

Sialidase
 CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

#### FIG. 52F

Insect cell expressed Reopro-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

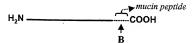
FIG. 52G

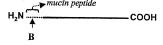
E. coli expressed Reopro-mucin fusion protein. a-e=0.

GalNAc Transferase, UDP-GalNAc
 CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 52H





$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_b \\ -(\mathrm{GalNAc-(Gal)_a-(Sia)_c-(R)_d} \end{bmatrix}_c$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 521

E. coli expressed Reopro-mucin fusion protein. a-e, n=0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

## FIG. 52J

E. coli expressed Reopro-mucin fusion protein. a-e, n = 0.

 GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
 ST3Gal3, asialo-transferrin
 CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

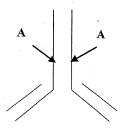
### FIG. 52K

E. coli expressed Reopro(N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

FIG. 52L



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i \\ \operatorname{GlcNAc} \\ (\operatorname{R}')_n \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_a)_e^- & (\operatorname{Sia})_i^- & (\operatorname{R})_v \\ (\operatorname{GlcNAc-(Gal)}_b)_i^- & (\operatorname{Sia})_i^- & (\operatorname{R})_w \\ (\operatorname{GlcNAc-(Gal)}_e)_g^- & (\operatorname{Sia})_i^- & (\operatorname{R})_v \\ (\operatorname{GlcNAc-(Gal)}_a)_h^- & (\operatorname{Sia})_m^- & (\operatorname{R})_y \\ \end{bmatrix}_{z=q}$$

a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotope-complex, drug, glycoconjugate.

R' = H, sugar, glycoconjugate.

FIG. 53A

### 245/498

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

```
    galactosyltransferase, UPD-Gal
    CMP-SA-toxin, ST3Gal3
```

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = toxin.
```

#### FIG. 53B

```
CHO, BHK, 293 cells, Vero or fungal expressed Rituxan. a, c, e, g, i, r, t (independently selected) = 0 or 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

galactosyltransferase,
 UPD-Gal-drug

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

### FIG. 53C

# 246/498

```
Fungi expressed Rituxan.

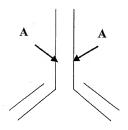
e, g, i, r, t (independently selected) = 0 or 1;

a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-radioisotope complex, ST3Gal3

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.
```

FIG. 53D



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & & \\ \operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{c} \cdot (\operatorname{Sia})_{j} \cdot (\mathbf{R})_{v} \\ \operatorname{GlcNAc-Gal})_{b} \mathbf{l}_{r} \cdot (\operatorname{Sia})_{k} \cdot (\mathbf{R})_{w} \end{bmatrix}_{i} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{r} \cdot (\operatorname{Sia})_{k} \cdot (\mathbf{R})_{w} \right]_{i} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{y} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\operatorname{Sia})_{m} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \mathbf{l}_{h} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \right]_{v} \\ \operatorname{Man} \left[ (\operatorname{GlcNAc-Gal})_{a} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})_{w} \cdot (\mathbf{R})$$

a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, glycoconjugate, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 53E

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

galactosyltransferase, UPD-Gal
 CMP-SA-PEG, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = PEG.
```

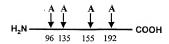
#### FIG. 53F

```
Fungi, yeast or CHO expressed Rituxan.
e, g, i, r, t, v, x (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u, w, y = 0; q, z = 1;
R (independently selected) = mannose, oligomannose, polymannose.
```

- 1. mannosidases (alpha and beta)
- 2. GNT-I,II, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal-radioisotope

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-radioisotope complex.
```

#### FIG. 53G



a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = mannose, polymer.

FIG. 54A

# 250/498

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
\begin{array}{lll} a\text{-d, i-m, q-u (independently selected)} = 0 \ or \ 1; \\ e\text{-h} = 1; \\ v\text{-y (independently selected)} = 1, \\ when j\text{-m (independently selected)} \ is \ 1; \\ R = PEG. \end{array}
```

#### FIG. 54B

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h=1; v-y=0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq)
```

```
    CMP-SA-PEG (1.2 mol eq),
    ST3Gal3
    CMP-SA (16 mol eq), ST3Gal3
```

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

### FIG. 54C

## 251/498

```
NSO expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- Galactosyltransferase, UDP-Gal
- ◆ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

#### FIG. 54D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
```

v-y (independently selected) = 0 or 1;

FIG. 54F

e-h = 1:

R = PEG.

### 252/498

CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H<sub>4</sub>N<sub>2</sub>-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

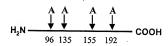
### FIG. 54F

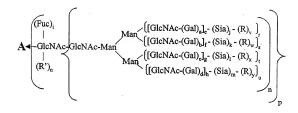
CHO, BHK, 293 cells, Vero expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, poly-α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 54G





a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100. R = polymer, linker, mannose. R' = H, sugar, glycoconjugate.

FIG. 54H

```
Insect, yeast or fungi cell expressed AT III.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
p = 1.

1. GNT 1, UDP-GlcNAc-PEG

a, i, q, r, -u (independently selected) = 0 or 1;
b-g, j-n, s-u, w-y = 0; p = 1;
v (independently selected) = 1,
```

when a (independently selected) is 1:

#### FIG. 541

R = PEG.

```
Yeast expressed AT III.

a-n=0; q-y (independently selected) = 0 to 1;

p=1;

R (branched or linear) = Man, oligomannose.
```

Endoglycanase
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

### FIG. 54J

# 255/498

CHO, BHK, 293 cells, Vero expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

- CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-transferrin.

FIG. 54K



$$(Fuc)_{i} \\ | \\ A \leftarrow GlcNAc \cdot GlcNAc \cdot Man \\ | \\ (R^{*})_{p} \\ | \\ (R^{*})_{q} \\ ([GlcNAc - (Gal)_{a}]_{e}^{-} \cdot (Sia)_{j}^{-} \cdot (R)_{v} \\ | \\ ([GlcNAc - (Gal)_{b}]_{f}^{-} \cdot (Sia)_{k}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{g}^{-} \cdot (Sia)_{l}^{-} \cdot (R)_{x} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{y} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^{-} \cdot (R)_{w} \\ | \\ ([GlcNAc - (Gal)_{d}]_{h}^{-} \cdot (Sia)_{m}^$$

a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer.

R', R" (independently selected) = sugar, glycoconjugate.

FIG. 54L

## 257/498

```
Yeast expressed AT III.
a-h, i-m, p, q = 0;
R (independently selected) = mannose,
oligomannose, polymannose;
r-u, v-y (independently selected) = 0 or 1;
n, o = 1.
```

- 1. endoglycanase
- ▼ 2. Galactosyltransferase, UDP-Gal-PEG

```
a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.
```

#### FIG. 54M

```
Plant expressed AT III.

a-d, f-h, j-m, p, s-u, v-y = 0;

e, i, q, r (independently selected) = 0 or 1;

n, o = l; R' = xylose.
```

- xylosidase
   Galactosyl transferase, UDP-
- Gal-PEG

b-d, f-h, j-m, p, q, s-u, w-y = 0; a, e, i, r (independently selected) = 0 or 1; n, o = 1; R = PEG.

# FIG. 54N

# 258/498

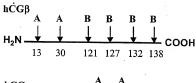
CHO, BHK, 293 cells, Vero, transgenic animal expressed AT III.
a-h, i-o, r-u (independently selected) = 0 or 1;

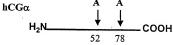
a-h, i-o, r-u (independently selected) = 0 or 1 p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 540





a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer

FIG. 55A

## 260/498

CHO, BHK, 293 cells, insect cell, Vero expressed hCG a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 to 1; r-u (independently selected) = 0 to 1; y-z = 0

1. Sialidase
2. CMP-SA-PEG, ST3Gal3

a-g, n, q = 1; h=1 to 3; i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; j-m, v-y (independently selected) = 0 or 1; R=PEG; z=0.

#### FIG. 55B

Insect cell, yeast, fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
2. CMP-SA-PEG. ST3Gal3

 $\begin{aligned} &b,\,d,\,f,\,h,\,k,\,m,\,o,\,p,\,s,\,u,\,w,\,y,\,z=0;\\ &a,\,c,\,e,\,g,\,i,\,n,\,q,\,r,\,t\,\,\,(independently\,selected)\\ &=0\,\,or\,\,1;\\ &j,\,l,\,v,\,x\,\,(independently\,selected)=0\,\,or\,\,1;\\ &R=PEG. \end{aligned}$ 

#### FIG. 55C

```
CHO, BHK, 293 cells, insect cell,
Vero expressed hCG
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.
```

- sialidase
- 2. CMP-SA, ST3Gal3
- 3. CMP-SA-PEG, ST3Gal1

```
a-h, i-o, q, r-u (independently selected) = 0 or 1; v-y = 0; p, z = 0 or 1; R = PEG.
```

#### FIG. 55D

```
CHO, BHK, 293 cells, insect cell or
Vero expressed hCG
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1; v-z = 0
```

#### 1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

### FIG. 55E

### 262/498

```
Insect cell, yeast or fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.
```

1. GNT's 1 and 2, UDP-GlcNAc-PEG

e, g, i, n, q, r, t, v, x (independently selected) = 0 or 1; a-d, f, h, j-m, o, p, s, w, y, z = 0; R = PEG.

### FIG. 55F

Insect cell, yeast or fungi expressed hCG
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t (independently selected)
= 0 or 1.

1. GNT-1, UDP-GlcNAc-PEG

e, i, n, q, r, v (independently selected) = 0 or 1; a-d, g, f, h, j-m, o, p, s, t, w-z = 0; R = PEG.

#### FIG. 55G

# 263/498

```
CHO, BHK, 293 cells, insect cell or

Vero expressed hCG
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
v-z = 0

1. CMP-SA-PEG, ST3Gal3
```

```
a-g, n, q = 1; h = 1 to 3;
i, o (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, p, z (independently selected) = 0 or 1;
R = PEG; v-y = 0.
```

#### FIG. 55H

```
CHO, BHK, 293 cells, Vero expressed hCG
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1; v-z = 0

1. CMP-SA-PEG, a2.8-ST
```

```
a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m (independently selected) = 0 to 2;

v-y (independently selected) = 1, when j-m

(independently selected) is 2; R = PEG; z = 0.
```

#### FIG. 551

# 264/498

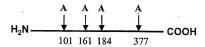
```
CHO, BHK, 293 cells, Vero expressed hCG a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to1; v-z = 0
```

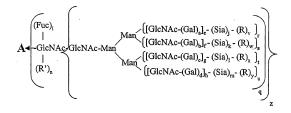
1. CMP-SA, poly-α2,8-ST

a-i, j-q, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-100; R = Sia.

FIG. 55J

### 265/498





a-d, i, n, q-u, z (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100; R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 56A

# 266/498

CHO, BHK, 293 cells, insect cells, Vero expressed and secreted alpha-galactosidase
a-h, i-m, q-u (independently selected) = 0 or 1;
z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

```
    Endo-H
    Galactosyltransferase, UDP-Gal-PEG-transferrin
```

```
a-h, i-m, q-u (independently selected) = 0 or 1;

n, v, y = 0; z = 1; and when z = 0 and q = 1,

then n (independently selected) = 0 or 1;

R' = Gal-PEG-transferrin.
```

#### FIG. 56B

```
CHO, BHK, 293 cells, Insect cells,
Vero expressed and secreted alpha-galactosidase
a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y
= 0; and when a-n = 0, then r-u (independently selected) = 0
or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.
```

```
1. Sialidase
2. CMP-SA-linker-Mannose-6-phosphate
```

```
a-h, i-m, q-u, v-y (independently selected) = 0 or 1;

n = 0; z = 1; R = mannose-6-phosphate; and when a-n

= 0, then r-u (independently selected) = 0 or 1;

v-y (independently selected) = 0-100;

R = mannose or mannose with mannose-6-phosphate.
```

### FIG. 56C

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NSO expressed alpha-galactosidase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0; Sia (independently selected) = Sia or Gal.

- 1. Sialidase and  $\alpha\mbox{-galactosidase}$
- Galactosyltransferase, UDP-Gal
   CMP-SA-linker-mannose-6-phosphate
   sialyltransferase

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = mannose-6 phosphate

#### FIG. 56D

CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-galactosidase
a-h, i-m, q-u (independently selected) = 0 or 1; z = 1;
n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

- 1. Sialidase
- 2. CMP-SA-PEG, sialyltransferase

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y = 0-100; R = mannose or mannose with mannose-6-phosphate.

#### FIG. 56E

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```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-galactosidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.
```

mannosyltransferase,
 GDP-mannose-linker-ApoE

```
 \begin{array}{ll} a\text{-}i=0; \ q\ (\text{independently selected})=0 \ \text{or}\ 1; \ z=1; \\ r\text{-}u\ (\text{independently selected})=0 \ \text{or}\ 1; \\ j\text{-}m\ (\text{independently selected})=0\text{-}100; \\ \text{Sia}=\text{mannose or mannose with mannose-6-phosphate;} \\ v\text{-}y\ (\text{independently selected})=0 \ \text{or}\ 1; \\ R=\text{mannose-linker-ApoE.} \end{array}
```

#### FIG. 56F

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-galactosidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate.

1. endo-H
2. galactosyltransferase,
UDP-Gal-linker-alpha2-macroglobulin
```

a-m, r-z = 0; n, q (independently selected) = 0 or 1; R' = galacotose-linker-alpha2-macroglobulin.

FIG. 56G

```
\begin{split} &\text{Insect cell, yeast, fungi expressed} \\ &\text{alpha-galactosidase.} \\ &\text{a-d, f, h, j-m, s, u, v-y} = 0; \\ &\text{e, g, i, q, r, t (independently selected)} = 0 \text{ or } 1. \end{split}
```

```
1. GNT-1,
UDP-GlcNAc-PEG-mannose-6-phosphate
```

```
e, i, q, r, v (independently selected) = 0 or 1;
a-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-mannose-6-phosphate.
```

### FIG. 56H

```
Insect cell, yeast, fungi expressed alpha-galactosidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

1. GNT-1, UDP-GlcNAc
2. galactosyltransferase,
UDP-Gal-PEG-transferrin

```
a, e, i, q, r, v (independently selected) = 0 or 1;
b-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-transferrin.
```

### FIG. 561

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Insect cell, yeast, fungi expressed alpha-galactosidase.

a-d, f, h, j-m, s, u, v-y=0;

e, g, i, q, r, t (independently selected) = 0 or 1.

- 1. GNT-1 and 2, UDP-GlcNAc
- 2. galactosyltransferase, UDP-Gal
- 3. sialyltransferase,

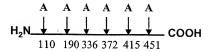
CMP-SA-PEG-melanotransferrin

a, c, e, g, i, j, l, q, r, t, v, x (independently selected) = 0 or 1;

b, d, f, h, k, m, n, s, u, w, y = 0;

z = 1; R = PEG-melanotransferrin.

FIG. 56J



a-d, i, n, q-u, z (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

v-y = 0 to 100;

R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 57A

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CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1:

n, v-y=0; and when a-n=0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

- Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG-transferrin

a-h, i-m, q-u (independently selected) = 0 or 1: n, v-y = 0; z = 1; and when z = 0 and q = 1, then n (independently selected) = 0 or 1; R' = Gal-PEG-transferrin.

#### FIG. 57B

CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase

a-h, i-m, q-u (independently selected) = 0 or 1: z = 1: n, v-y=0; and when a-n=0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

- Sialidase
- 2. CMP-SA-linker-Mannose-6-phosphate ST3Gal3

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0z = 1; R = mannose-6-phosphate; and when a - n = 0,

then r-u (independently selected) = 0 or 1;

v-v (independently selected) = 0-100:

R = mannose or mannose with mannose-6-phosphate.

#### **FIG 57C**

NSO expressed alpha-iduronidase.
a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1;
v-y = 0; Sia (independently selected) = Sia or Gal.

- Sialidase and α-galactosidase
- Galactosyltransferase, UDP-Gal
- 3. CMP-SA-linker-mannose-6-phosphate sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate
```

### FIG. 57D

CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

- 1. Sialidase
- 2. CMP-SA-PEG, sialyltransferase

```
a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

### FIG. 57E

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```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-iduronidase.
a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate.
```

```
    mannosyltransferase,
    GDP-mannose-linker-ApoE
```

```
a-i = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate; v-y (independently selected) = 0 or 1; R = mannose-linker-ApoE.
```

#### FIG. 57F

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-iduronidase.

a-i, v-y = 0; q (independently selected) = 0 or 1;

z = 1; r-u (independently selected) = 0 or 1;

j-m (independently selected) = 0-100;

Sia = mannose or mannose with mannose-6-phosphate.
```

```
    endo-H
    galactosyltransferase,
    UDP-Gal-linker-alpha2-macroglobulin
```

```
a-m, r-z = 0; n, q (independently selected) = 0 or 1; R' = galacotose-linker-alpha2-macroglobulin.
```

### FIG. 57G

```
Insect cell, yeast, fungi expressed alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT-1,
UDP-GlcNAc-PEG-mannose-6-phosphate
```

```
e, i, q, r, v (independently selected) = 0 or 1;
a-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-mannose-6-phosphate.
```

### FIG. 57H

```
Insect cell, yeast, fungi expressed
alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

1. GNT-1, UDP-GlcNAc
2. galactosyltransferase,
UDP-Gal-PEG-transferrin

```
a, e, i, q, r, v (independently selected) = 0 or 1; b-d, f-h, j-n, s-u, w-y = 0; z = 1; R = PEG-transferrin.
```

### FIG. 571

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```
Insect cell, yeast, fungi expressed alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- GNT-1 and 2, UDP-GlcNAc
   galactosyltransferase, UDP-Gal
   sialyltransferase,
   CMP-SA-PEG-melanotransferrin
- a, c, e, g, i, j, l, q, r, t, v, x (independently selected) = 0 or 1; b, d, f, h, k, m, n, s, u, w, y = 0; z = 1; R = PEG-melanotransferrin.

FIG. 57J

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#### FIG. 58A

ACCCCCTGGGCCCTGCCAGCTCCCTGCCCCAGAGCTTCCTGCTCAAT
GCTTAGAGCAAGTGAGGAAGATCCAGGGCGATGGCGCAGCGCTCCAG
GAGAAGCTGTGTGCCACCCAAGAGCTGTGCCACCCCAGAGAGCTTGGT
GCTGCTCGGGACACTCTCTGGGCATCCCTTGAGCCAACTCCATA
GCGGCCTTTTCCTCTACCAGGGGCTCCTGCAGGCCTGGAAGGGATCT
CCCCCAGTTGGGTCCCACCTTGGACACACTGCAGCTGGACGTCCCA
ACTTTGCCACACACTCTGGCAGCAGTGGAAGACTTGCCC
CCTGCCTGCAGCCCACCCAGGGTGCCATGCAGCTCGCCTTCCCTTCCT
TTCCAGCGCCGGCAGGAGGGTCCTGGTTGCCTCCATCTGCAGAG
CTTCCTGGAGGTGCCACCCTTGCCACCCTTGCAGAG
CTTCCTGGAGGTGCCACCCAGGCTTCCCCATCTGCAGAG
CTTCCTGGAGGTGCTACCGCGCTTCACCCAGCCCTTG
A

#### FIG. 58B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Glin Ser Phe Leu Leu Lys Cys Leu Glu Glin Val Arg Lys Ile Glin Gly Asp Gly Ala Ala Leu Glin Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Glin Ala Leu Glin Leu Ala Gly Cys Leu Ser Glin Leu His Ser Gly Leu Phe Leu Tyr Glin Gly Leu Leu Glin Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Glin Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Glin Glin Met Glu Glu Leu Gly Met Ala Pro Ala Leu Glin Pro Thr Glin Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Glin Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Glin Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Glin Pro

# 278/498 FIG. 59A

GCGCCTCTTATGTACCCACAAAAATCTATTTTCAAAAAAGTTGCTCTA AGAATATAGTTATCAAGTTAAGTAAAATGTCAATAGCCTTTTAATTTA ATTTTTAATTGTTTTATCATTCTTTGCAATAATAAAACATTAACTTTAT ACTTTTTAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA TAGATACACAGTGTATATGTGATTAAAATATAATGGGAGATTCAATC AATAATGAAAAAATGTGGTGAGAAAACAGCTGAAAACCCATGTA AAGAGTGTATAAAGAAAGCAAAAAGAGAAGTAGAAAGTAACACAGG GGCATTTGGAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA CCTTTGCTTTACTGGTGGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT GCTCTGTGGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTTCTCC TGCTTGAAGGACAGACATGACTTTGGATTTCCCCAGGAGGAGTTTGG CAACCAGTTCCAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA GACTCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT TCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCTTGT GCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTCTTTGTCA ACAAACTTGCAAGAAAGTTAAGAAGTAAGGAATGAAAACTGGTTCA ACATGGAAATGATTTCATTGATTCGTATGCCAGCTCACCTTTTTATG ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT TAAATCTTTTCAAATGTTTTTAGGAGTATTAATCAACATTGTATTCAG ATCTATTTAAATATTTTTAAAAATATTATTTATTTAACTATTTATAAAAAC AACTTATTTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA CATTGAACTTTTGCTATGGAACTTTTGTACTTGTTTATTCTTTAAAATG AAATTCCAAGCCTAATTGTGCAACCTGATTACAGAATAACTGGTACA TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACC TAACAAATACAATTCTGCTCTCTTGTGTATTTGATTTTGTATGAAAA AAACTAAAAATGGTAATCATACTTAATTATCAGTTATGGTAAATGGT ATGAAGAGAAGAAGGAACG

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#### FIG. 59B

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu

#### FIG. 59C

#### FIG. 59D

Met Ala Leu Leu Phe Pro Leu Leu Ala Ala Leu Val Met Thr Ser Tyr Ser Pro Val Gly Ser Leu Gly Cys Asp Leu Pro Gln Asn His Gly Leu Leu Ser Arg Asn Thr Leu Val Leu Leu His Gln Met Arg Arg Ile Ser Pro Phe Leu Cys Leu Lys Asp Arg Arg Asp Phe Arg Phe Pro Gln Glu Met Val Lys Gly Ser Gln Leu Gln Lys Ala His Val Met Ser Val Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe His Thr Glu Arg Ser Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln Leu His Thr Gly Leu His Gln Gln Leu Gln His Leu Gly Glu Gly Glu Gly Glu Ser Ala Gly Ala Ile Ser Ser Pro Ala Leu Thr Leu Larg Arg Tyr Phe Gln Gly Ile Arg Val Tyr Leu Lys Glu Lys Lys Tyr Ser Asp Cys Ala Trp Glu Val Val Arg Met Glu Ile Met Lys Ser Leu Phe Leu Ser Thr Asn Met Gln Glu Arg Leu Arg Ser Lys Asp Arg Asp Leu Gly Ser Ser

#### FIG. 60A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC ACTACAGCTCTTTCCATGAGCTACAACTTGCTTGGATTCCTACAAGA AGCAGCAATTTTCAGTGTCAGAAGCTCCTGTGGCAATTGAATGGGAG GCTTGAATATTGCCTCAAGGACAGGATGAACTTTGACATCCCTGAGG AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCATTGACC ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA TGTCTATCATCAGATAAACCATCTGAAGACAGTCCTGGAAGAAAAC TGGAGAAAGAAGATTTTACCAGGGGAAAACTCATGAGCAGTCTGCAC CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA ACTTTTACTTCATTAACAGACTTACAGGTTACCTCCGAAACTGAAGAT CTCCTAGCCTGTCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC AACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCAAAT GAAAGGACACTAGAAGATTTTGAAATTTTTATTAAATTATGAGTTATT TTTATTTAT TTAAATTTTATTTTGGAAAATAAATTATTTTTGGTGC

#### FIG. 60B

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly ArgLeu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

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#### FIG. 61A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG GGCTGCCTGGCTGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT CCTGCACCGGCGCGCGCGCCAACGCGTTCCTGGAGGAGCTGCGGC CGGGCTCCCTGGAGAGGAGGAGGAGGAGCAGTGCTCCTTCGA GGAGGCCCGGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC TGGATTTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA GAATGGGGGCTCCTGCAAGGACCAGCTCCAGTCCTATATCTGCTTCT GCCTCCCTGCCTTCGAGGGCCGGAACTGTGAGACGCACAAGGATGAC CAGCTGATCTGTGAACGAGAACGGCGGCTGTGAGCAGTACTGCAG TGACCACACGGGCACCAAGCGCTCCTGTCGGTGCCACGAGGGGTACT CTCTGCTGGCAGACGGGGTGTCCTGCACACCCACAGTTGAATATCCA TGTGGAAAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAACCCCA AGGCCGAATTGTGGGGGGCAAGGTGTGCCCCAAAGGGGAGTGTCCA TGGCAGGTCCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGGAC CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC CTCAGCGAGCACGACGGGATGAGCAGAGCCGGCGGGTGGCGCAGG GCGCTGCTCCGCCTGCACCAGCCCGTGGTCCTCACTGACCATGTGGTG CCCCTCTGCCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC GTGCGCTTCTCATTGGTCAGCGGCTGGGGCCAGCTGCTGGACCGTGG CGCCACGGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT ATCACGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA CTCCTGCAAGGGGACAGTGGAGGCCCACATGCCACCCACTACCGGG GCACGTGGTACCTGACGGGCATCGTCAGCTGGGGCCAGGGCTGCGCA ACCGTGGGCCACTTTGGGGTGTACACCAGGGTCTCCCAGTACATCGA GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCCTCC TGCGAGCCCCATTTCCC

#### FIG. 61B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cvs Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tvr Met Phe Cvs Ala Gly Tvr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

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#### FIG. 62A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAAGCCTCATCAC CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTTTCTT GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA GTATGGAAGAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA AACACTGAAAAGACAACTGAATTTTGGAAGCAGTATGTTGATGGAGA TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG ACATTAATTCCTATGAATGTTGGTGTCCCTTTGGATTTGAAGGAAAGA ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT GCCATTTCCATGTGGAAGAGTTTCTGTTTCACAAACTTCTAAGCTCAC CCGTGCTGAGGCTGTTTTTCCTGATGTGGACTATGTAAATCCTACTGA AGCTGAAACCATTTTGGATAACATCACTCAAGGCACCCAATCATTTA ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA TTCCCTTGGCAGGTTGTTTTGAATGGTAAAGTTGATGCATTCTGTGGA GGCTCTATCGTTAATGAAAAATGGATTGTAACTGCTGCCCACTGTGTT GAAACTGGTGTTAAAATTACAGTTGTCGCAGGTGAACATAATATTGA GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT ATTCCTCACCACAACTACAATGCAGCTATTAATAAGTACAACCATGA CATTGCCCTTCTGGAACTGGACGAACCCTTAGTGCTAAACAGCTACG TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCCTCA AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA GGGAGATCAGCTTTAGTTCTTCAGTACCTTAGAGTTCCACTTGTTGAC CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT GTTCTGTGCTGGCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG ATAGTGGGGGACCCCATGTTACTGAAGTGGAAGGGACCAGTTTCTTA ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAATA TGGAATATACCAAGGTATCCCGGTATGTCAACTGGATTAAGGAAA AAACAAAGCTCACTTAATGAAAGATGGATTTCCAAGGTTAATTCATT GGAATTGAAAATTAACAG

#### FIG. 62B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cvs Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asp Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tvr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

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#### FIG. 63A

#### FIG. 63B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Sèr Ala Pro Asp Val Ghn Asp Cys Pro Glu Cys Thr Leu Ghn Glu Asn Pro Phe Phe Ser Ghn Pro Gly Ala Pro Ile Leu Ghn Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Ghn Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

#### FIG. 63C

#### FIG. 63D

Met Lys Thr Leu Gin Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

#### FIG. 64A

CCCGGAGCCGGGCCACCGCGCCCGCTCTGCTCCGACACCGC GCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT GCACCGCCGAGCTTCCCGGGATGAGGGCCCCCGGTGTGGTCACCCGG CGCGCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGGAGATGGGG GTGCACGAATGTCCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTCG CTCCCTCTGGGCCTCCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT GACAGCCGAGTCCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG AGAATATCACGACGGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT ATCACTGTCCCAGACACCAAAGTTAATTTCTATGCCTGGAAGAGGAT GGAGGTCGGGCAGCAGGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG CTGTCGGAAGCTGTCCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC CAGCCGTGGGAGCCCCTGCAGCTGCATGTGGATAAAGCCGTCAGTGG CCTTCGCAGCCTCACCACTCTGCTTCGGGCTCTGCGAGCCCAGAAGG AAGCCATCTCCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA ATCACTGCTGACACTTTCCGCAAACTCTTCCGAGTCTACTCCAATTTC CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG GGGACAGATGACCAGGTGTGTCCACCTGGGCATATCCACCACCTCCC TCACCAACATTGCTTGTGCCACACCCTCCCCGCCACTCCTGAACCCC GTCGAGGGGCTCTCAGCTCAGCGCCAGCCTGTCCCATGGACACTCCA GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC AACTCTGAGATCTAAGGATGTCACAGGGCCAACTTGAGGGCCCAGAG CAGGAAGCATTCAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC AGGACACGCTTTGGAGGCGATTTACCTGTTTTCGCACCTACCATCAGG GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG GTCTCACGGGCATGGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCTCTGG CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA ACTGAAACCACCAAAAAAAAAAAAA

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#### FIG. 64B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Ala Glu Ass Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Leu Glu Ala Lys Glu Ala Glu Ass Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

#### FIG. 65

Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Lyr Thr Gly Glu Ala Cys Arg Thr Gly Asp

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### FIG. 66A

### FIG. 66B

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Gln Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

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#### FIG. 67A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACACTGCAGGACCCATATGTAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTCAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTTGGAAAGAAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAATTGTCTCCTTTTACTTCAAACT
TITTAAAAACTTTAAAGATGACCAGAGCCTCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAG
AAACGAGATGACTTCGAAAAGCATCAATTATTCGGTAACTGACTT
GAATGTCCAACGCAAAGCATCACATGAACTCATCAAGTGATGGCTG
AACTGTCGCAGCACAAACAAAAGGAGATGACTCATCAAGTGATGGCTG
GACTGTCGCCAGCAGCTAAAACAGGAAGCGAAAAAGGAGTCAGAT
GCTGTTTCGAGGTCGAAGAGCATCCCAGTAA

### FIG. 67B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gin Leu Cys Ile Val Leu Gly Ser Leu Gly Cys Tyr Cys Gin Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gin Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gin Lys Ser Val Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala Ile His Glu Leu Ile Gin Val Met Ala Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln

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### FIG. 68A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGGCATCCT CCTGCTGGCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTGAGGA TCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCACCATGATC AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC GCCTTCAGCCTATACCGCCAGCTGGCACACCCAGTCCAACAGCACCAA TATCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTGA ATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTC GACCACCGGCAATGGCCTGTTCCTCAGCGAGGGCCTGAAGCTAGTGG ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC ACTGTCAACTTCGGGGACACCGAAGAGGGCCAAGAACAGATCAACG ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT. AAAGGCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG AAGCGTTTAGGCATGTTTAACATCCAGCACTGTAAGAAGCTGTCCAG CTGGGTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT TCCTGCCTGATGAGGGGAAACTACAGCACCTGGAAAATGAACTCACC CACGATATCATCACCAAGTTCCTGGAAAATGAAGACAGAAGGTCTGC CAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAA GAGCGTCCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG CTGACCTCTCCGGGGTCACAGAGGAGGCACCCCTGAAGCTCTCCAAG GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC TGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATCCCCCCCGA GGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATAC AACTGCCTCTCGCTCCTCAACCCCTCCCTCCATCCCTGGCCCCCTCC CTGGATGACATTAAAGAAGGGTTGAGCTGG

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#### FIG. 68B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn Lvs Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gin Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr Gln Lvs

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#### . FIG. 69A-1

GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT GTTTAGTGGATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAAGTCCTTCCA AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCGTGGGCATCAGGT GCCCGCCCTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCCGACCTTTCCT GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG GCCTGCTACTGACCCTGCAGCCAGAACAGAAGTTCCAGAAAGTGAAG GGATTTGGAGGGCCATGACAGATGCTGCTGCTCTCAACATCCTTGCC CTGTCACCCCCTGCCCAAAATTTGCTACTTAAATCGTACTTCTCTGAA GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTTCCA GTTGCACAACTTCAGCCTCCCAGAGGAAGATACCAAGCTCAAGATAC CCCTGATTCACCGAGCCCTGCAGTTGGCCCAGCGTCCCGTTTCACTCC TTGCCAGCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG GTGAATGGGAAGGGTCACTCAAGGGACAGCCCGGAGACATCTACC ACCAGACCTGGGCCAGATACTTTGTGAAGTTCCTGGATGCCTATGCTG AGCACAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT GCTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTCACCCCT GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCCTACCCTCGCC AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGC TTGCTGCCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC AGCTAAATATGTTCATGGCATTGCTGTACATTGGTACCTGGACTTTCT GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCCTGTTCCCCA ACACCATGCTCTTTGCCTCAGAGGCCTGTGTGGGCTCCAAGTTCTGGG AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGGATGCAGTACAGC CACAGCATCATCACGAACCTCCTGTACCATGTGGTCGGCTGGACCGAC TGGAACCTTGCCCTGAACCCCGAAGGAGGACCCAATTGGGTGCGTAA CTTTGTCGACAGTCCCATCATTGTAGACATCACCAAGGACACGTTTTA CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC TGAGGGCTCCCAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTCG TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG CTGTGGGCTTCCTGGAGACAATCTCACCTGGCTACTCCATTCACACCT ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG GCTCAGCCTGGGCATTAAAGGGACAGAGTCAGCTCACACGCTGTCTG TGACTAAAGAGGGCACAGCAGGGCCAGTGTGAGCTTACAGCGACGT

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### FIG. 69A-2

AAGCCCAGGGGCAATGGTTTGGGTGACTCACTTTCCCCTCTAGGTGGT GCCCAGGGCTGGAGGCCCCTAGAAAAAGATCAGTAAGCCCCAGTGTC CCCCCAGCCCCCATGCTTATGTGAACATGCGCTGTTGTGTTGCTT TGGAAACT

#### FIG. 69B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Gln Ala Val Ser Trp Ala Ser Glv Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tvr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asp Ser Thr His His Asp Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

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#### FIG. 70A

ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGCTGCTGTGTGG AGCAGTCTTCGTTTCGCCCAGCCAGGAAATCCATGCCCGATTCAGAA GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAAACGCA GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA GCAACCGGGTGGAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC CACTCAGTGCCTGTCAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG GGGCACCTGCCAGCAGGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG CCCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAGGGCCA CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC AGCGGAGAGTGCCCGAGTGCACCAACTGGAACAGCAGCGCGTTG GCCCAGAAGCCCTACAGCGGGCGGAGGCCAGACGCCATCAGGCTGG GCCTGGGGAACCACAACTACTGCAGAAACCCAGATCGAGACTCAAA GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGCTCAGAGTTCT GCAGCACCCCTGCCTGCTCTGAGGGAAACAGTGACTGCTACTTTGGG AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC CTCCTGCCTCCCGTGGAATTCCATGATCCTGATAGGCAAGGTTTACAC AGCACAGAACCCCAGTGCCCAGGCACTGGGCCTGGGCAAACATAATT ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG GAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCT TTGCCAAGCACAGGAGGTCGCCGGGAGAGCGGTTCCTGTGCGGGGGC ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG GAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAA TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGA GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTG CCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGC CTTGTCTCCTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACT GTACCCATCCAGCCGCTGCACATCACAACATTTACTTAACAGAACAG TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCC CAGGCAAACTTGCACGACGCCTGCCAGGGCGATTCGGGAGGCCCCCT GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG GTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGACC AGGAACACCCGACTCCTCAAAAGCAAATGAGATCC

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### FIG. 70B

Met Asn Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly Ala Val Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asp Met Arg Pro

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#### FIG. 71A

ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA TGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTG TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAACAAAGAAA ACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTG AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC ATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTC AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA GCTCAAAGCAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAA TATCAACGTAATAGTTCTGGAACTAAAGGGATCTGAAACAACATTCA TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA AATATTTAAATTTTATTTTTTTTTTGAATGTATGGTTGCTACCTATTG TAACTATTATTCTTAATCTTAAAACTATAAATATGGATCTTTTATGAT CAAAAATATTATTATTATGTTGAATGTTAAATATAGTATCTATGTAG AAACAAAAAAAAAA

#### FIG. 71B

Met Tyr Arg Met Gin Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gin Leu Gin Leu Glu His Leu Leu Asp Leu Gin Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Giu Leu Lys Gin Leu Gin Cys Leu Gin Giu Giu Leu Lys Pro Leu Giu Giu Val Leu Asn Leu Ala Gin Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Giy Ser Giu Thr Thr Phe Met Cys Giu Tyr Ala Asp Giu Thr Ala Thr Ile Val Giu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gin Ser Ile Ile Ser Thr Leu Thr

### FIG. 72A-1

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ATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTGCGATTCT GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCA TGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG ATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT GTACAAAAAGACTCTGTTTGTAGAATTCACGGATCACCTTTTCAACAT CGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCC AGGCTGAGGTTTATGATACAGTGGTCATTACACTTAAGAACATGGCT TCCCATCCTGTCAGTCTTCATGCTGTTGGTGTATCCTACTGGAAAGCT TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAG AAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCTGGCAG GTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC CTACTCATATCTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGG CCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGG AAAAGACACAGACCTTGCACAAATTTATACTACTTTTTTGCTGTATTTG ATGAAGGGAAAAGTTGGCACTCAGAAACAAGAACTCCTTGATGCA GGATAGGGATGCTGCATCTGCTCGGGCCTGGCCTAAAATGCACACAG TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAA GTGCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCAT CGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCCTTACTGCTCAA ACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCATATCTCTT CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG ACTATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG ATGATGACAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGA AGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGAC TGGGACTATGCTCCCTTAGTCCTCGCCCCGATGACAGAAGTTATAAA AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA AAAAGTCCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTG AAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG TCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTCCAAT TCTGCCAGGAGAAATATTCAAATATAAATGGACAGTGACTGTAGAAG ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC TCCTCATCTGCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATA ATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAAC CGAAGCTGGTACCTCACAGAGAATATACAACGCTTTCTCCCCAATCCA GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT GCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTGTCAGTTTG TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTGGAGCACAGA CTGACTTCCTTTCTCTCTCTGGATATACCTTCAAACACAAAAT

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### FIG. 72A-2

GGTCTATGAAGACACACTCACCCTATTCCCATTCTCAGGAGAAACTGT CTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCCACA ACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCT AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCAAAAGCAATTT AATGCCACCACAATTCCAGAAAATGACATAGAGAAGACTGACCCTTG GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA GTGATTTGTTGATGCTCTTGCGACAGAGTCCTACTCCACATGGGCTAT CCTTATCTGATCTCCAAGAAGCCAAATATGAGACTTTTTCTGATGATC CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA CACTTCAGGCCACAGCTCCATCACAGTGGGGACATGGTATTTACCCC TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAACTGGGGACAACTG CAGCAACAGAGTTGAAGAAACTTGATTTCAAAGTTTCTAGTACATCA AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT GATAATACAAGTTCCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT AGTCAATTAGATACCACTCTATTTGGCAAAAAGTCATCTCCCCTTACT GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATAATGATTCAAA GTTGTTAGAATCAGGTTTAATGAATAGCCAAGAAAGTTCATGGGGAA AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGAAAAGA GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGTT AGCATCTCTTTGTTAAAGACAAACAAACTTCCAATAATTCAGCAACT AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG TCCATCAGTCTGGCAAAATATATTAGAAAGTGACACTGAGTTTAAAA AAGTGACACCTTTGATTCATGACAGAATGCTTATGGACAAAAATGCT ACAGCTTTGAGGCTAAATCATATGTCAAATAAAACTACTTCATCAAA AAACATGGAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACTCTCTGAA CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCAG GTAGTAGGAAAGGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA TGGTTTTTCCAAGCAGCAGAAACCTATTTCTTACTAACTTGGATAATT TACATGAAAATAATACACACAATCAAGAAAAAAAAAATTCAGGAAGA AATAGAAAAGAAGGAAACATTAATCCAAGAGAATGTAGTTTTGCCTC AGATACATACAGTGACTGGCACTAAGAATTTCATGAAGAACCTTTTC TTACTGAGCACTAGGCAAAATGTAGAAGGTTCATATGACGGGGCATA TGCTCCAGTACTTCAAGATTTTAGGTCATTAAATGATTCAACAAATAG AACAAAGAAACACACAGCTCATTTCTCAAAAAAAGGGGAGGAAGAA AACTTGGAAGGCTTGGGAAATCAAACCAGCAAATTGTAGAGAAATAT GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAATTTTG TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA

### FIG. 72A-3

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GAAGAAACAGAACTTGAAAAAAGGATAATTGTGGATGACACCTCAAC CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCTCACAC AGATAGACTACAATGAGAAGGAGAAAGGGGCCATTACTCAGTCTCCC TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA TCTCCATTACCCATTGCAAAGGTATCATCATCTATTAGACCTA TATATCTGACCAGGGTCCTATTCCAAGACAACTCTTCTCATCTTCCAG CAGCATCTTATAGAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT TTCTTACAAGGAGCCAAAAAAAAAAATAACCTTTCTTTAGCCATTCTAACC TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACACTGTTCTCCC GAAACCAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA CAGAGGGAGCGATTAAGTGGAATGAAGCAAACAGACCTGGAAAAGT GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAGAAAAAAACAGCT TTTAAGAAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAAGCAAT CATGCAATAGCAGCAATAAATGAGGGACAAAATAAGCCCGAAATAG AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA AACCCACCAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGT TGAAATGAAGAAGGAAGATTTTGACATTTATGATGAGGATGAAAATC AGAGCCCCCGCAGCTTTCAAAAGAAAACACGACACTATTTTATTGCTG CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT GGAGAACTAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC AGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTC GTCCCTATTCCTTCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG GCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAACCA AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT GAGTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA AAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACT AACACACTGAACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT TGCTCTGTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT GAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGA CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA TTCGATGGTATCTGCTCAGCATGGGCAGCAATGAAAACATCCATTCT ATTCATTTCAGTGGACATGTGTTCACTGTACGAAAAAAAGAGGAGTA TAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTGAGACAGTGGA

### FIG. 72A-4

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AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATTGG CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA TAAGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT TCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGG CCAGACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAG CCCTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC GGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACAT CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG TGGATTCATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTG CTCGATACATCCGTTTGCACCCAACTCATTATAGCATTCGCAGCACTC TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGA CTTCACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA CAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTAT GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC TCTCTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGA CTCCTTCACACCTGTGGTGAACTCTCTAGACCCACCGTTACTGACTCG CTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCCTGAG GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC CACTGCAGCACCTGCCACTGCCGTCACCTCTCCCTCAGCTCCAGG GCAGTGTCCCTCCCTGGCTTGCCTTCTACCTTTGTGCTAAATCCTAGC AGACACTGCCTTGAAGCCTCCTGAATTAACTATCATCAGTCCTGCATT TCTTTGGTGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTCTTA CCTATTTCTGCAGCTGCTCCCAGATTACTCCTTCCTTCCAATATAACT AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG AAAAGTTAGGCCTCTCAGAGTCACCACTTCCTCTGTTGTAGAAAAACT ATGTGATGAAAACTTTGAAAAAGATATTTATGATGTTAACATTTCAGGT TAAGCCTCATACGTTTAAAATAAAACTCTCAGTTGTTTATTATCCTGA TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT GGAGTCAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA TACAATAACTACTACAGTAAAGTCTGTTTCTGCTTCCTTACACATAGA TATAATTATGTTATTTAGTCATTATGAGGGGCACATTCTTATCTCCAA AACTAGCATTCTTAAACTGAGAATTATAGATGGGGTTCAAGAATCCC TAAGTCCCCTGAAATTATATAAGGCATTCTGTATAAATGCAAATGTGC ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATTCT GACCAATAAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG AAATGATGA

# FIG. 72B-1 302/498

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asn Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tvr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asp Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe

FIG. 72B-2

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Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Glv Asp Tvr Tvr Glu Asp Ser Tvr Glu Asp Ile Ser Ala Tvr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly Lvs Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu Lvs Thr Asn Lvs Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Glv Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr Val Thr Gly Thr Lvs Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro

# FIG. 72B-3 304/498

Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr Tvr Lvs Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu As Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn lle His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile

FIG. 72B-4

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Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gin Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro. Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr

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#### FIG. 73A

TCCACCTGTCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG GCGCGCCTGCTTCTCTGCGTCCTGGTCGTGAGCGACTCCAAAGGCAGC AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA ACATGTGTGTCCAACAGTACTTCTCCAACATTCACTGGTGCAACTGC CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAC CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG ACACCATGGGCCGGCCCTGCCTGCCCTGGAACTCTGCCACTGTCCTTC AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG GGAAACATAATTACTGCAGGAACCCAGACAACCGGAGGCGACCCTGG TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCCAAGAGTGCATGGT GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCCTCCCAGAAGAAT TAAAATTTCAGTGTGGCCAAAAGACTCTGAGGCCCCGCTTTAAGATTA TTGGGGGAGAATTCACCACCATCGAGAACCAGCCCTGGTTTGCGGCC ATCTACAGGAGGCACCGGGGGGGCTCTGTCACCTACGTGTGTGGAGG CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTCGCTCAA GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAC CTCATCCTACACAAGGACTACAGCGCTGACACGCTTGCTCACCACAAC GACATTGCCTTGCTGAAGATCCGTTCCAAGGAGGGCAGGTGTGCGCA GCCATCCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAGAGA ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA AGCTGATTTCCCACCGGGAGTGTCAGCAGCCCCACTACTACGGCTCTG AAGTCACCACAAAATGCTGTGTGCTGCTGACCCACAGTGGAAAACA GATTCCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC GGGTCCCCAGGGAGGAAACGGGCACCACCCGCTTTCTTGCTGGTTGTC ATTTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA AGAT

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### FIG. 73B

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cvs Val Leu Val Val Ser Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cvs Asp Cvs Leu Asn Glv Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu Gln Gln Thr Tvr His Ala His Arg Ser Asn Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asn Asn Arg Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Île Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asp Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

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#### FIG.74A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA TAGACTACTTTTTTTTTTTAAGCAGCAAAAAGGAGAAAATTGTCATCA AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC ACCATCATCTCAGGATGAGGGGCATGAAGCTGCTGGGGGGCGCTGCTG GCACTGGCGGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC CTTCAACATCCAGACATTTGGGGAGACCAAGATGTCCAATGCCACCCT CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCGTGTA CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACGATGATG GTCAGGTTCTCCCCGGTTCACAGAGGTCAGGGAGTTTGCCATTGTT CCCCTGCATGCGGCCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGCTTGGAGGACG TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT CCCAGTGGTCATCCGCCTGTGGACAAGCCCCACCTTCCAGTGGC TGATCCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT ATGACAGGATCGTGGTTGCAGGGATGCTGCTCCGAGGCGCCGTTGTTC CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG CTGAAGTGAGCAGCCCTCCCCACACCAGTTGAACTGCAG

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### FIG. 74B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala IIe Ser Asp His Tyr Pro Val Glu Val Met Leu Lys

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#### FIG. 75A

### FIG. 75B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly lle Val Glu Glin Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

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#### FIG. 76A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCCT GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC GGGCCAGGGTTCACCCCACCACACGGCGGTCTTTTGGGGTGGAGCCC TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCCTG TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA TTCCACCAAGCTCTGCTAGATCCCAGAGTGAGGGGCCTATATTTTCCT GCTGGTGGCTCCAGTTCCGGAACAGTAAACCCTGTTCCGACTACTGTC TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC ATGGAGAGCACAACATCAGGATTCCTAGGACCCCTGCTCGTGTTACA GGCGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCACAGAGTCT AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTT ATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTC TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCCTCTACTTCCAGGAA CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCCTGCT CAAGGAACCTCTATGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGAC GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA GTGCCATTTGTTCAGTGGTTCGCAGGGCTTTCCCCCACTGTTTGGCTTT CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT TGAGTCCCTTTTTACCTCTATTACCAATTTTCTTTTGTCTTTGGGTATAC ATTTGA

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#### FIG. 76B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile Lvs Val Glv Ala Glv Asp Phe Glv Pro Glv Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Thr Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile

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### FIG. 77A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCCTTATCCAGGC CTTTTGACAACGCTATGCTCCGCGCCCATCGTCTGCACCAGCTGGCCT TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG AAGTATTCATTCCTGCAGAACCCCCAGACCTCCCTCTGTTTCTCAGAG TCTATTCCGACACCCTCCAACAGGGAGGAAACACACACAGAAATCCAA CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTCGTGGCTGGA GCCCGTGCAGTTCCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAAACTCACA CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG GAAGGACATGGCAAGGTCGAGACATTCCTGCGCATCGTGCAGTGCCG CTCTGTGGAGGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG TGACCCCTCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACTCCAGT GCCCACCAGCCTTGTCCTAATAAAATTAAGTTGCATC

#### FIG. 77B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln CysArg Ser Val Glu Gly Ser Cys Gly Phe

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#### FIG. 78A

TTATCTTTTGTCCTTGCTGCTCATTGGCTTCTGGGACTGCGTGACCTGT CACGGGAGCCTGTGGACATCTGCACAGCCAAGCCGCGGGACATTCC CATGAATCCCATGTGCATTTACCGCTCCCGGAGAAGAAGGCAACTG AGGATGAGGCTCAGAACAGAAGATCCCGGAGGCCACCAACCGGCG TGTCTGGGAACTGTCCAAGGCCAATTCCCGCTTTGCTACCACTTTCTA TCAGCACCTGGCAGATTCCAAGAATGACAATGATAACATTTTCCTGTC ACCCCTGAGTATCTCCACGGCTTTTGCTATGACCAAGCTGGGTGCCTG TAATGACACCTCCAGCAACTGATGGAGGTATTTAAGTTTGACACCAT ATCTGAGAAACATCTGATCAGATCCACTTCTTCTTTGCCAAACTGAA CTGCCGACTCTATCGAAAAGCCAACAAATCCTCCAAGTTAGTATCAGC CAATCGCCTTTTTGGAGACAAATCCCTTACCTTCAATGAGACCTACCA GGACATCAGTGAGTTGGTATATGGAGCCAAGCTCCAGCCCCTGGACT TCAAGGAAAATGCAGAGCAATCCAGAGCGGCCATCAACAAATGGGTG TCCAATAAGACCGAAGCCGAATCACCGATGTCATTCCCTCGGAAGC CATCAATGAGCTCACTGTTCTGGTGCTGGTTAACACCCATTTACTTCAA TGTTCTACAAGGCTGATGGAGAGTCGTGTTCAGCATCTATGATGTACC AGGAAGGCAAGTTCCGTTATCGGCGCGTGGCTGAAGGCACCCAGGTG CTTGAGTTGCCCTTCAAAGGTGATGACATCACCATGGTCCTCATCTTG CCCAAGCCTGAGAAGAGCCTGGCCAAGGTGGAGAAGGAACTCACCCC AGAGGTGCTGCAGGAGTGGCTGGATGAATTGGAGGAGATGATGCTGG TGGTCCACATGCCCCGCTTCCGCATTGAGGACGGCTTCAGTTTGAAGG AGCAGCTGCAAGACATGGGCCTTGTCGATCTGTTCAGCCCTGAAAAG TCCAAACTCCCAGGTATTGTTGCAGAAGGCCGAGATGACCTCTATGTC TCAGATGCATTCCATAAGGCATTTCTTGAGGTAAATGAAGAAGGCAG TGAAGCAGCTGCAAGTACCGCTGTTGTGATTGCTGGCCGTTCGCTAAA CCCCAACAGGGTGACTTTCAAGGCCAACAGGCCTTTCCTGGTTTTTAT AAGAGAAGTTCCTCTGAACACTATTATCTTCATGGGCAGAGTAGCCA ACCCTTGTGTTAAGTAA

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#### FIG. 78B

Met Tyr Ser Asn Val Ile Gly Thr Val Thr Ser Gly Lys Arg Lys Val Tyr Leu Leu Ser Leu Leu Ile Gly Phe Trp Asp Cys Val Thr Cys His Gly Ser Pro Val Asp Ile Cys Thr Ala Lys Pro Arg Asp Ile Pro Met Asn Pro Met Cys Ile Tyr Arg Ser Pro Glu Lys Lys Ala Thr Glu Asp Glu Gly Ser Glu Gln Lys Ile Pro Glu Ala Thr Asn Arg Arg Val Trp Glu Leu Ser Lys Ala Asn Ser Arg Phe Ala Thr Thr Phe Tyr Gln His Leu Ala Asp Ser Lys Asn Asp Asn Asp Asn Ile Phe Leu Ser Pro Leu Ser Ile Ser Thr Ala Phe Ala Met Thr Lys Leu Gly Ala Cys Asn Asp Thr Leu Gln Gln Leu Met Glu Val Phe Lys Phe Asp Thr Ile Ser Glu Lys Thr Ser Asp Gln Ile His Phe Phe Phe Ala Lys Leu Asn Cys Arg Leu Tyr Arg Lys Ala Asn Lys Ser Ser Lys Leu Val Ser Ala Asn Arg Leu Phe Gly Asp Lys Ser Leu Thr Phe Asn Glu Thr Tvr Gln Asp Ile Ser Glu Leu Val Tyr Gly Ala Lys Leu Gln Pro Leu Asp Phe Lys Glu Asn Ala Glu Gln Ser Arg Ala Ala Ile Asn Lys Trp Val Ser Asn Lys Thr Glu Gly Arg Ile Thr Asp Val Ile Pro Ser Glu Ala Ile Asn Glu Leu Thr Val Leu Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Leu Trp Lys Ser Lys Phe Ser Pro Glu Asn Thr Arg Lys Glu Leu Phe Tyr Lys Ala Asp Gly Glu Ser Cys Ser Ala Ser Met Met Tyr Gln Glu Gly Lys Phe Arg Tyr Arg Arg Val Ala Glu Gly Thr Gln Val Leu Glu Leu Pro Phe Lys Gly Asp Asp Ile Thr Met Val Leu Ile Leu Pro Lys Pro Glu Lys Ser Leu Ala Lys Val Glu Lys Glu Leu Thr Pro Glu Val Leu Gln Glu Trp Leu Asp Glu Leu Glu Glu Met Met Leu Val Val His Met Pro Arg Phe Arg lle Glu Asp Gly Phe Ser Leu Lys Glu Gln Leu Gln Asp Met Gly Leu Val Asp Leu Phe Ser Pro Glu Lys Ser Lys Leu Pro Gly Ile Val Ala Glu Gly Arg Asp Asp Leu Tyr Val Ser Asp Ala Phe His Lys Ala Phe Leu Glu Val Asn Glu Glu Gly Ser Glu Ala Ala Ala Ser Thr Ala Val Val Ile Ala Gly Arg Ser Leu Asn Pro Asn Arg Val Thr Phe Lys Ala Asn Arg Pro Phe Leu Val Phe Ile Arg Glu Val Pro Leu Asn Thr Ile Ile Phe Met Gly Arg Val Ala Asn Pro Cys Val Lys

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### FIG. 79A

ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCG
GTGTTTCTGCATGTCCATTCCGCTCCTGATGTGCAGGATTGCCCAG
AATGCACGCTACAGGAAAACCCATTCTTCTCCCAGCCGGGTGCCCCA
ATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCATATCCCACTCCA
CTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGA
GTCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGG
GGGTTTCAAAGTGGAGAACCACACGGCGTGCCACTGCAGTACTTGTT
ATTATCACAAATCTTAA

### FIG. 79B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

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### FIG. 79C

ATGAGATGTTCCAGGGCTGCTGCTGTTGCTGCTGAGCATGGGC
GGGACATGGGCATCCAAGGAGCCGCTTCGGCCACGGTGCGCCCCCAT
CAATGCCACCCTGGCTGTGGAGAAGAGGGCTGCCCCGTTGCATCA
CCGTCAACACCACCATCTGTGCCGGCTACTGCCCCACCATGACCCGCG
TGCTGCAGGGGTCCTGCCGGCCCTCAGGTGGTGCAACTACC
GCGATGTGCGCTTCGAGTCCATCCGGCTCCCTGGCTGCCCGCCGGCG
TGAACCCCGTGCTCTACGCCGTTCCATGCTGCAACTACC
CTGACCTGCGACACCACTGACTGCAGCTCCAAGGACCACCCC
TTGACCTGTGATGACCCCCGCTTCCAGGACTCCTCTCAAAGGCC
CCTCCCCCCAGCCTTCCAAGCCCATCCCGACTCCCGGGGGCCTTGGAC
ACCCCGATCCTCCAACACCATCCCGACTCCCGGGGCCCTCGGAC
ACCCCGATCCCCCACAATAA

#### FIG. 79D

Met Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Leu Ser Met Gly Gly Thr Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn Ala Thr Leu Ala Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr Val Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg Val Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg Asp Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val Asn Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu Cys Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu Thr Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln

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ATGCGTCCCCTGCGCCCCGCGCGCGCTGCTGGCGCTCCTGGCCTCG CTCCTGGCCGCCCCCGGTGGCCCCGGCCGAGGCCCCGCACCTGGT GCAGGTGGACGCGCCCGCGCGCTGTGGCCCCTGCGGCGCTTCTGGA GGAGCACAGGCTTCTGCCCCCCGCTGCCACACAGCCAGGCTGACCAG TACGTCCTCAGCTGGGACCAGCAGCTCAACCTCGCCTATGTGGGCGCC GTCCCTCACCGCGCATCAAGCAGGTCCGGACCCACTGGCTGCTGGA GCTTGTCACCACCAGGGGGTCCACTGGACGGGGCCTGAGCTACAACT TCACCCACCTGGACGGGTACTTGGACCTTCTCAGGGAGAACCAGCTCC TCCCAGGGTTTGAGCTGATGGGCAGCGCCTCGGGCCACTTCACTGACT TTGAGGACAAGCAGCAGGTGTTTGAGTGGAAGGACTTGGTCTCCAGC CTGGCCAGGAGATACATCGGTAGGTACGGACTGGCGCATGTTTCCAA GTGGAACTTCGAGACGTGGAATGAGCCAGACCACCACGACTTTGACA ACGTCTCCATGACCATGCAAGGCTTCCTGAACTACTACGATGCCTGCT GGCGACTCCTTCCACACCCCACCGCGATCCCCGCTGAGCTGGGGCCTC CTGCGCCACTGCCACGACGGTACCAACTTCTTCACTGGGGAGGCGGG CGTGCGGCTGGACTACATCTCCCTCCACAGGAAGGGTGCGCGCAGCT CCATCTCCATCCTGGAGCAGGAGAAGGTCGTCGCGCAGCAGATCCGG CAGCTCTTCCCCAAGTTCGCGGACACCCCCATTTACAACGACGAGGCG GACCCGCTGGTGGGCTGGTCCCTGCCACAGCCGTGGAGGCCGGACGT GACCTACGCGCCATGGTGGTGAAGGTCATCGCGCAGCATCAGAACC TGCTACTGGCCAACACCACCTCCGCCTTCCCCTACGCGCTCCTGAGCA ACGACAATGCCTTCCTGAGCTACCACCCGCACCCCTTCGCGCAGCGCA CGCTCACCGCGCGCTTCCAGGTCAACACCCCGCCGCCGCCGCACGTG CAGCTGTTGCGCAAGCCGGTGCTCACGGCCATGGGGCTGCTGGCGCT GCTGGATGAGGAGCAGCTCTGGGCCGAAGTGTCGCAGGCCGGGACCG TCCTGGACAGCACCACGGTGGGCGTCCTGGCCAGCGCCCACCGC CCCCAGGGCCGGCGACGCCTGGCGCGCGCGGTGCTGATCTACGC GAGCGACGACCCGCGCCCCACCCCAACCGCAGCGTCGCGGTGACCC TGCGGCTGCGCGGGTGCCCCCGGCCCGGGCCTGGTCTACGTCACG CGCTACCTGGACAACGGGCTCTGCAGCCCCGACGGCGAGTGGCGCG CCTGGGCCGGCCGTCTTCCCCACGGCAGAGCAGTTCCGGCGCATGC GCGCGGCTGAGGACCCGGTGGCCGCGCGCCCCCTTACCCGCC GGCGGCCGCCTGACCCTGCGCCCCGCGCTGCGGCTGCCGTCGCTTTTG CTGGTGCACGTGTGCGCCCCGAGAAGCCGCCCGGGCAGGTCAC GCGGCTCCGCGCCCTGCCCCTGACCCAAGGGCAGCTGGTTCTGGTCTG GTCGGATGAACACGTGGGCTCCAAGTGCCTGTGGACATACGAGATCC AGTTCTCTCAGGACGGTAAGGCGTACACCCCGGTCAGCAGGAAGCCA TCGACCTTCAACCTCTTTGTGTTCAGCCCAGACACAGGTGCTGTCTCT GGCTCCTACCGAGTTCGAGCCCTGGACTACTGGGCCCGACCAGGCCC CTTCTCGGACCCTGTGCCGTACCTGGAGGTCCCTGTGCCAAGAGGGCC CCCATCCCCGGGCAATCCAT GA

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#### FIG. 80B

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val Gln Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro

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### FIG. 81A

ATGCAGCTGAGGAACCCAGAACTACATCTGGGCTGCGCGCTTGCGCT TCGCTTCCTGGCCCTCGTTTCCTGGGACATCCCTGGGGCTAGAGCACT AGCGCTTCATGTGCAACCTTGACTGCCAGGAAGAGCCAGATTCCTGC ATCAGTGAGAAGCTCTTCATGGAGATGGCAGAGCTCATGGTCTCAGA AGGCTGGAAGGATGCAGGTTATGAGTACCTCTGCATTGATGACTGTTG GATGGCTCCCCAAAGAGATTCAGAAGGCAGACTTCAGGCAGACCCTC AGCGCTTTCCTCATGGGATTCGCCAGCTAGCTAATTATGTTCACAGCA AAGGACTGAAGCTAGGGATTTATGCAGATGTTGGAAATAAAACCTGC GCAGGCTTCCCTGGGAGTTTTGGATACTACGACATTGATGCCCAGACC TTTGCTGACTGGGGAGTAGATCTGCTAAAATTTGATGGTTGTTACTGT GACAGTTTGGAAAATTTGGCAGATGGTTATAAGCACATGTCCTTGGCC CTGAATAGGACTGGCAGAAGCATTGTGTACTCCTGTGAGTGGCCTCTT TATATGTGGCCCTTTCAAAAGCCCAATTATACAGAAATCCGACAGTAC TGCAATCACTGGCGAAATTTTGCTGACATTGATGATTCCTGGAAAAGT ATAAAGAGTATCTTGGACTGGACATCTTTTAACCAGGAGAGAATTGTT GATGTTGCTGGACCAGGGGGTTGGAATGACCCAGATATGTTAGTGAT TGGCAACTTTGGCCTCAGCTGGAATCAGCAAGTAACTCAGATGGCCCT CTGGGCTATCATGGCTGCTCCTTTATTCATGTCTAATGACCTCCGACA CATCAGCCCTCAAGCCAAAGCTCTCCTTCAGGATAAGGACGTAATTGC CATCAATCAGGACCCCTTGGGCAAGCAAGGGTACCAGCTTAGACAGG GAGACAACTTTGAAGTGTGGGAACGACCTCTCTCAGGCTTAGCCTGG GCTGTAGCTATGATAAACCGGCAGGAGATTGGTGGACCTCGCTCTTAT ACCATCGCAGTTGCTTCCCTGGGTAAAGGAGTGGCCTGTAATCCTGCC TGCTTCATCACACACCTCCTCCCTGTGAAAAGGAAGCTAGGGTTCTAT GAATGGACTTCAAGGTTAAGAAGTCACATAAATCCCACAGGCACTGT TTTGCTTCAGCTAGAAAATACAATGCAGATGTCATTAAAAGACTTACT TTAA

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#### FIG. 81B

Met Gln Leu Arg Asn Pro Glu Leu His Leu Gly Cys Ala Leu Ala Leu Arg Phe Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu Asp Asn Gly Leu Ala Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu Arg Phe Met Cys Asn Leu Asp Cys Gln Glu Glu Pro Asp Ser Cys Ile Ser Glu Lys Leu Phe Met Glu Met Ala Glu Leu Met Val Ser Glu Gly Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp Cys Trp Met Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln Arg Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala Asp Trp Gly Val Asp Leu Leu Lys Phe Asp Gly Cys Tyr Cys Asp Ser Leu Glu Asn Leu Ala Asp Gly Tyr Lys His Met Ser Leu Ala Leu Asn Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro Leu Tyr Met Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys Ser Ile Leu Asp Trp Thr Ser Phe Asn Gin Glu Arg Ile Val Asp Val Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp Met Leu Val Ile Gly Asn Phe Gly Leu Ser Trp Asn Gln Gln Val Thr Gin Met Ala Leu Trp Ala Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp Leu Arg His Ile Ser Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala Ile Asn Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala Met Ile Asn Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala Val Ala Ser Leu Gly Lys Gly Val Ala Cys Asn Pro Ala Cys Phe Ile Thr Gln Leu Leu Pro Val Lys Arg Lys Leu Gly Phe Tyr Glu Trp Thr Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr Val Leu Leu Gln Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu

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#### FIG. 82A

ATGGCGCCGTCGCCGTCTGGGCCGCCGTCGGACTGGAGCT CTGGGCTGCGCCACGCCTTGCCCGCCCAGGTGGCATTTACACCCTA CGCCCGGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG GACAGCACATACACCCAGCTCTGGAACTGGGTTCCCGAGTGCTTGAG  $\tt CTGTGGCTCCGGTGTAGCTCTGACCAGGTGGAAACTCAAGCCTGCAC$ TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG CGCTGAGCAAGCAGGAGGGGTGCCGGCTGTGCGCAAG TGCCGCCCGGGCTTCGGCGTGGCCAGACCAGGAACTGAAACATCAGA CGTGGTGTCAAGCCCTGTGCCCCGGGGACGTTCTCCAACACGACTTC ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGGCCAT CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCACGTCCCCCA ACACGATCCCAACACACGCAGCCAACTCCAGAACCCAGCACTGCTCC AAGCACCTCCTTCCTGCTCCCAATGGGCCCCAGCCCCCAGCTGAAGG GAGCACTGGCGACTTCGCTCTTCCAGTTGGACTGATTGTGGGTGTGAC AGCCTTGGGTCTACTAATAATAGGAGTGGTGAACTGTGTCATCATGAC CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC CTCACTTGCCTGCCGATAAGGCCCGGGGTACACAGGGCCCCGAGCAG CAGCACCTGCTGATCACAGCGCCGAGCTCCAGCAGCAGCTCCCTGGA GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC CACAGGCACCAGGCGTGGAGGCCAGTGGGGCCGGGGAGGCCCGGGC CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCCAGG TCAATGTCACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT CACAGTGCTCCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC AGCCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCTTCTCCAAGGA GGAATGTGCCTTTCGGTCACAGCTGGAGACGCCAGAGACCCTGCTGG GGAGCACCGAAGAGAAGCCCCTGCCCCTTGGAGTGCCTGATGCTGGG ATGAAGCCCAGTTAACCAGGCCGGTGTGGGCTGTGTCGTAGCCAAGG TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTT CCAGGC

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### FIG. 82B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gin Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser

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### FIG. 83A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

#### FIG. 83B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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#### FIG. 84A

Gin Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gin Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gin Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

#### FIG. 84B

Asp Ile Gin Met Thr Gin Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gin Leu Ser Val Gly Tyr Met His Trp Tyr Gin Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gin Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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#### FIG. 85A

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGTGAGTCCAGGA
GAAAGAGTCAGTTTCTCCTGCAGGGCCAGTCAGTTCGTTTGGCTCAAGC
ACACACTGGTATCAGCAAAGAACAAATGGTTCTCCAAGGCTTCTCATA
AAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCCAGGTTTAGTGGC
AGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT
GAAGATATTGCAGATTATTACTGTCAACACAAGTCATAGCTGGCCATTC
ACGTTCGGCTCGGGGACAAATTTGGAAGTAAAAGAAGTCATGAAGCTTGA
GGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTCT
CCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGG
TCCACCAGTCTCCAGAGAAGGGGCTTGATTGGTTGCTGAAATTAGA
TCAAAATCTATTAATTCTGCAACACTTATGGCGGCTTGTGAAAGGG
AGGTTCACCATCTCAAGAGATGATTCCAAAAGTGCTGTCTACCTGCAA
ATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG
AATTACTACGGTAGTACCTACGACTACTGGGGCCAAGGCACCACTCTC
ACACGTCTCC

#### FIG. 85B

Asp Ile Leu Leu Thr Gin Ser Pro Ala Ile Leu Ser Val·Ser Pro Gly Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gin Phe Val Gly Ser Ser Ile His Trp Tyr Gin Gin Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gly Thr Thr Leu Thr Val Ser

#### FIG. 86A

ATGGAGACAGACACTCCTGTTATGGGTGCTGCTGCTCTGGGTTCCA GGTTCCACTGGTGACGTCAGGCGAGGCCCCGGAGCCTGCGGGGCAG GGACGCCCAGCCCCACGCCCTGCGTCCCGGCCGAGTGCTTCGACC TGCTGGTCCGCCACTGCGTGGCCTGCGGGCTCCTGCGCACGCCGCGGC CGAAACCGGCCGGGCCAGCAGCCCTGCGCCCAGGACGCGCTGCAG CCGCAGGAGTCGGTGGGCGCGGGGGGCGGCGGCGGCGGCGACA AAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGA CCGTCAGTCTTCCCCCCCAAAACCCAAGGACACCCTCATGATC TCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGA AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGC ATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTA CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGG CAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA TCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT CAGCCTGACCTGCTCAAAGGCTTCTATCCCAGCGACATCGCCGT GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACG CCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTC ACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCTCCCGGGAAATGA

#### FIG. 86B

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

#### FIG. 87

Asp lle Gin Met Thr Gin Thr Thr Ser Ser Leu Ser Ala Ser Leu Giy Asp Arg Val Thr lle Ser Cys Arg Ala Ser Gin Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gin Gin Lys Pro Asp Giy lle Val Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Giy Val Pro Ser Arg Phe Ser Giy Ser Giy Ser Giy Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Giu Gin Gin Asp Ile Ala Thr Tyr Phe Cys Gin Gin Giy Asn Thr Leu Pro Trp Thr Phe Giy Giy Giy Thr Lys Leu Giu Ile Lys

#### FIG. 88

Gin Val Gin Leu Gin Gin Ser Gly Ala Glu Leu Val Gly Pro Gly Thr Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu lle Glu Trp Val Lys Gln Arg Pro Gly Gin Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ala

#### FIG. 89

Asp Ile Gin Met Thr Gin Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gin Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gin Gin Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gin Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gin Gin Gly Asn Thr Leu Pro Trp Thr Phe Gly Gin Gly Thr Lys Val Glu Val Lys

#### FIG. 90

Gin Val Gin Leu Val Gin Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gin Ala Pro Gly Gin Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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#### FIG. 91

Asp Ile Gin Met Thr Gin Thr Pro Ser Thr Leu Ser Ala Ser Val Giy Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gin Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gin Gin Lys Pro Giy Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Giy Val Pro Ser Arg Phe Ser Giy Ser Giy Ser Giy Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gin Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gin Gin Giy Asn Thr Leu Pro Trp Thr Phe Giy Gin Giy Thr Lys Val Giu Val Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Giu Gin Leu Lys Ser Giy Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Giu Ala Lys Val Gin Trp Lys Val Asp Asn Ala Leu Gin Ser Giy Asn Ser Gin Giu Ser Val Thr Giu Gin Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Giu Lys His Lys Val Tyr Ala Cys Giu Val Thr His Gin Giy Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Giy Giu Cys

#### FIG. 92

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Glv

#### FIG. 93A

ATGGATTTTCAGGTGCAGATTATCAGCTTCCTGCTAATCAGTGCTTCA GTCATAATGTCCAGAGGGCAAATTGTTCTCTCCCAGTCTCCAGCAATC CTGTCTGCATCTCCAGGGGAGAAGGTCACAATGACTTGCAGGGCCAG CTCAAGTGTAAGTTACATCCACTGGTTCCAGCAGAAGCCAGGATCCTC CCCCAAACCCTGGATTTATGCCACATCCAACCTGGCTTCTGGAGTCCC TGTTCGCTTCAGTGGCAGTGGGTCTGGGACTTCTTACTCTCTCACAAT CAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAGCAGT GGACTAGTAACCCACCCACGTTCGGAGGGGGGACCAAGCTGGAAATC AAA

#### FIG. 93B

Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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#### FIG. 94A

ATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTACGCGTGTCCTGTCCACGGTGACACACTGCAGCAGCAGCCTGGGGCTGAGCTGGTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGACACCTGGTCGGGGCCTGGAATGGATTGAAGGCTATTTATCCCGGAAATGGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGCCACATTGACTGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCACAGCACTCTGCAGCTCACTGCAGCTCACTGCAGCTCACTGCAGCTCACTGCAGCTCACTGCAGCTTACTACTGCGGTGACTGGTACTTCAAATGTCTGGGGCGCAGGGACCACGGTCACCGTCACCGTCTCTTGCA

#### FIG. 94B

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Asp Trp Tyr Phe Asn Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala

### 333/498 FIG. 95A

GACGTCGCGGCCGCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGGGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATTGGCTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGC GGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACCATGAGGGTCCCCGCTCAGCTCCT GGGGCTCCTGCTCTGGCTCCCAGGTGCACGATGTGATGGTACCAA GGTGGAAATCAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCT GCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGG ATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAG GACAGCAAGGACACCTACAGCCTCAGCAGCACCCTGACGCTGAG CAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCC ATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAG TGTTGAATTCAGATCCGTTAACGGTTACCAACTACCTAGACTGGATTC GTGACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTG CCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCT TGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGG AAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTG GGGTGGGCAGGACAGCAAGGGGGGGGGATTGGGAAGACAATAGCAG GCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGAC AGCTATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGC CCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGT TTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGA 

### 334/498 FIG. 95B

CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC CTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

#### FIG. 95C

GCTGCGATTTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTG GTAGGATTTTATCCCCGCTGCCATCATGGTTCGACCATTGAACTGCAT CGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAACGGAGACCTAC CCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACC ACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAG GAAAACCTGGTTCTCCATTCCTGAGAACAATCGACCTTTAAAGGACA GAATTAATATAGTTCTCAGTAGAGAACTCAAAGAACCACCACGAGGA GCTCATTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTTATTGAA CAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGG CAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTTAGACT CTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCC AGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCG TCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAA GTCTACGAGAAGAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGC TCCCCTCCTAAAGTCATGCATTTTTATAAGACCATGGGACTTTTGCTG TTGCCCCTCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCAC TGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG GTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGG AGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCT ATGGAACCAGCTGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTT ATTTGCATAATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCA GTAGTTGATTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACA GTGTTCTCTGCACAGATAAGGACAAACATTATTCAGAGGGAGTACCC AGAGCTGAGACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGA AATATGCTTGTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGG TAAGGGCCAATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGG CAGAGCATATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTC TGACATAGTTGTGTGGGAGCTTGGATCGATCCTCTATGGTTGAACAA GATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTC GGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGA CCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTAT CGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTG TCACTGAAGCGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGG CAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATC ATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGC CCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATC AGGGGCTCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG CCCGACGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCG

### 336/498 FIG. 95D

AATATCATGGTGGAAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGC CGGCTGGGTGTGGCGACCGCTATCAGGACATAGCGTTGGCTACCCG TGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT GCTTTACGGTATCGCCGCTTCCCGATTCGCAGCGCATCGCCTTCTATC GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGAC CGACCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCCACCG CCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCG GCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCC ACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA GCATCACAAATTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTT GTGGTTTGTCCAAACTCATCAATCTATCTTATCATGTCTGGATCGCGG CCGCGATCCCGTCGAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCC TGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGG AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTC GGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGA GCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGC TGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATC GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATAC CAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACC CTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA CACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTA ACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGA AGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAA CAAACCACCGCTGGTAGCGGTGGTTTTTTTTTTTTTGCAAGCAGCAGATT ACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTCTAC GGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGG TCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA AATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTG ACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTC TATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC GAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCA GCCGGAAGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTC 

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#### FIG. 95E

CAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGG
TGTCACGCTCGTCGTGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAAC
GATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTT
AGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTG
TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC
CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCAT
CTGAGAATAGTGTTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAA
TACGGGATAATACCGCCCACATAGCAGAACTTTAAAAGTGCTCATC
ATTGGAAAACGTTCTTCGGGGGGAAAACTCTCAAGGATCTTCA
GCATCTTTTACTTTCACAGCTTTCTGGGTGACCCAACTGATCTTCA
GCATCTTTTACTTTCACAGCGTTTCTGGGTGACCCAACAGAACTGATCTTCA
GCATCTTTTACTTTCACAGCGTTTCTTGGGTGAGCAAAAACAGGAAGG
CAAAATGCCGCAAAAAAGGGAATATTATTATTATAGAAACTTTTACAGGGTTA
TACTCATACTCTTTCTTTTCAATATTATTAGAAACATTTATCAAGGGTTA
TTGTCTCATGAGCGGAACATATTTCCCGAAAAATGTCCACCT

## 338/498 FIG. 96A

GACGTCGCGGCCGCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGCGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATTGGCTGGTTAGGGGCGGGACTATGGTTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTTGGCAGTACATCAATGGGCGTGGATACC GGTTTGACTCACGCGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACTATGGATTTTCAGGTGCAGATTAT CAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAAT TGTTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAA GGTCACAATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATCCACT GGTTCCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTATGCCA CATCCAACCTGGCTTCTGGAGTCCCTGTTCGCTTCAGTGGCAGTGGGT CTGGGACTTCTTACTCTCTCACAATCAGCAGAGTGGAGGCTGAAGATG GAGGGGGACCAAGCTGGAAATCAAACGTACGGTGGCTGCACCATCT GTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC TCTGTTGTGTGCCTGAATAACTTCTATCCCAGAGAGGCCAAAGTA CAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG TGTCACAGAGCAGGACAGCAGCACCTACAGCCTCAGCAGCA CCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTT CAACAGGGGAGAGTGTTGAATTCAGATCCGTTAACGGTTACCAACTA CCTAGACTGGATTCGTGACAACATGCGGCCGTGATATCTACGTATGAT CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTC CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCC

### 339/498 FIG. 96B

TAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCT ATTCTGGGGGTGGGGTGGGCAGGACAGCAAGGGGGAGGATTGGG AAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCA GCTGGGGCTCGACAGCTATGCCAAGTACGCCCCCTATTGACGTCAATG ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCAT GGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTG ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT TGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACT CCGCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTC TATATAAGCAGAGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGA ACACAGACCCGTCGACATGGGTTGGAGCCTCATCTTGCTCTTGT CGCTGTTGCTACGCGTGTCCTGTCCCAGGTACAACTGCAGCAGCCTGG GGCTGAGCTGGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG CTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGA CACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCCGGAAAT GGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGGCCACATTGAC TGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGA CATCTGAGGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACG GCGGTGACTGGTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACC GTCTCTGCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCC TCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT CAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGG GCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC AAGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGG TCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAG ACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACA AGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACC ATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCT GCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCT GGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAA GAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATG AGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG GTAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGT

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#### FIG. 96C

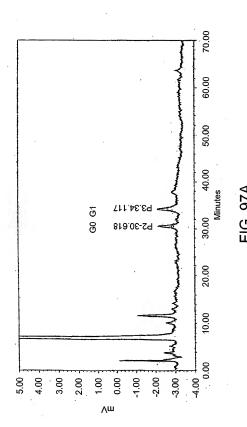
GACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCC ACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAA ATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG GTGGGGCAGGACAGCAAGGGGGGGGGGGATTGGGAAGACAATAGCAGGC ATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAG CGCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCAT AATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGA TTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCAGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGGGCTGCGATTTCG CGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTGGTAGGATTTTATC CCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCC CAAAATATGGGGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCT CAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACAACCTCTTCAG TGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTC TCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTT CTCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTCTTGC CAAAAGTTTGGATGATGCCTTAAGACTTATTGAACAACCGGAATTGG CAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCTGTTTACC AGGAAGCCATGAATCAACCAGGCCACCTTAGACTCTTTGTGACAAGG ATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTG GGGAAATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGA GGTCCAGGAGAAAAAGGCATCAAGTATAAGTTTGAAGTCTACGAGA AGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCCTAA AGCTATGCATTTTATAAGACCATGGGACTTTTGCTGGCTTTAGATCA CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT TCTGGGGGGTGGGGGGGGGGGGGAGGATTGGGAA GACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGC TGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTTATTTGCATAATG GCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCTGCA CAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAGACT CCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTTGTC ATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCCAAT CTGCTCACACAGGATAGAGAGGCAGGAGCAGGAGCATATA AGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAGTTG

### 341/498 FIG. 96D

TGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAAGATGGATTGCA CGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTG GGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTC AGCGCAGGGGCCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGC CGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGG GAAGGGACTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTG TCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCA ATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCAC CAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGG TCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGC CAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAG GATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTG GAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTG GCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGA AGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTAT CGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGA GCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGA AAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCT CCAGCGCGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTT TATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT CACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAA ACTCATCAATCTATCTTATCATGTCTGGATCGCGGCCGCGATCCCGTC GAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTG TAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTT GCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGC GCTCTTCCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCT GCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCA CAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCA GCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCC ATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA ATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAA GCTGGGCTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC

FIG. 96E

GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC TTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAACCACCGC TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAA AAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGC TCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATC AAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAA ATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATG CTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTC CGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTA TGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCT TTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACC GCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCG ATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAA AAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCT TTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC GCACATTTCCCCGAAAAGTGCCACCT



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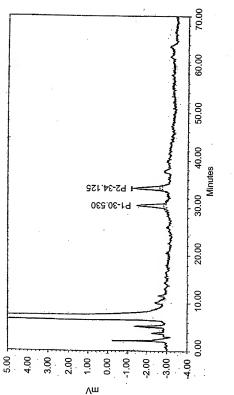


FIG. 97B

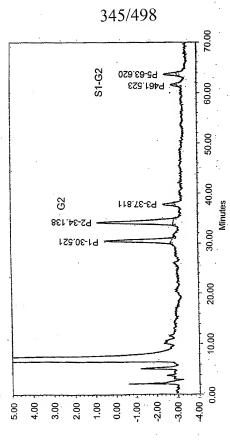


FIG. 97C

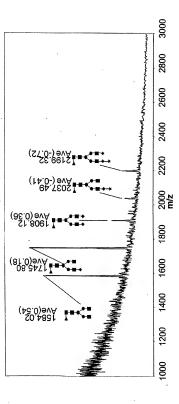
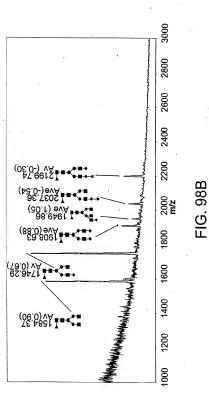


FIG. 98A



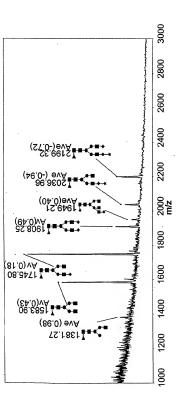
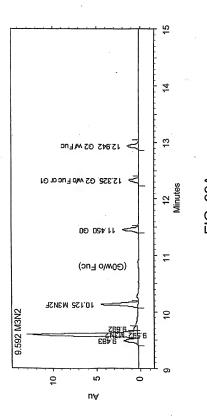
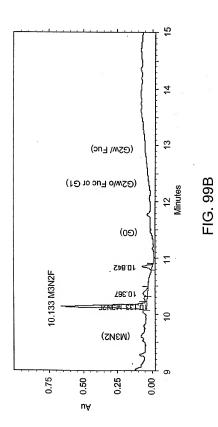
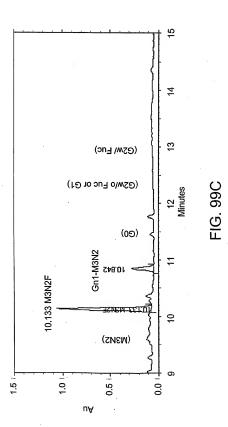


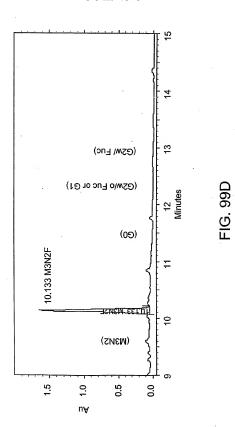
FIG. 98C







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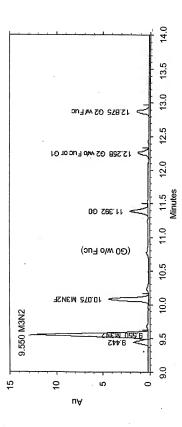
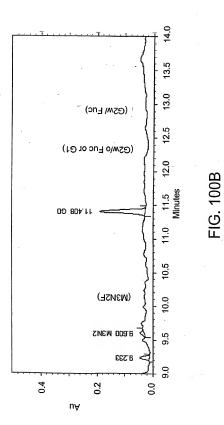
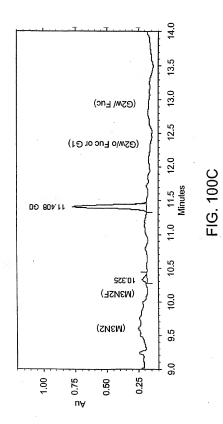
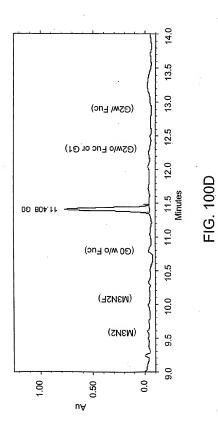


FIG. 100A







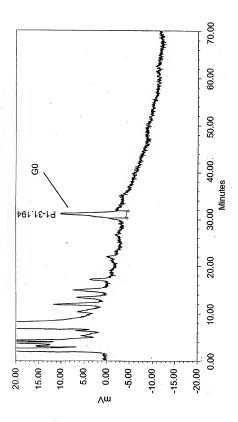


FIG. 101A

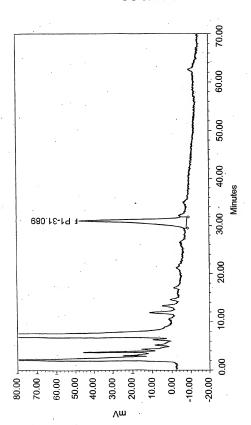
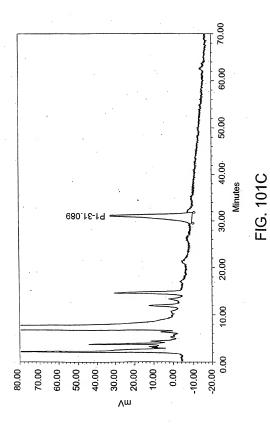


FIG 101B



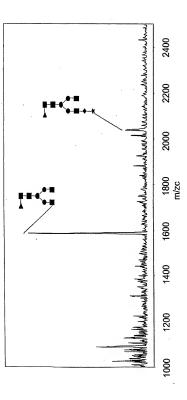


FIG. 102A

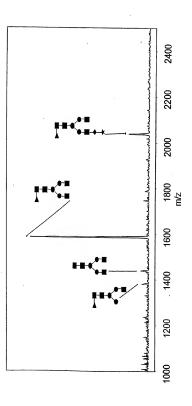


FIG. 102B

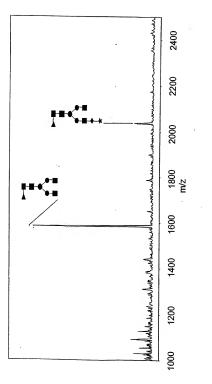


FIG. 102C

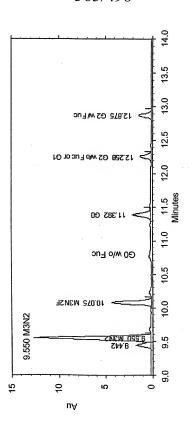


FIG. 103A

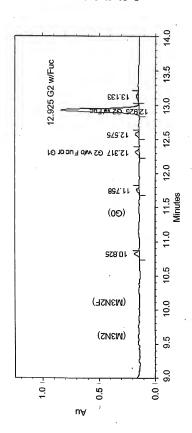
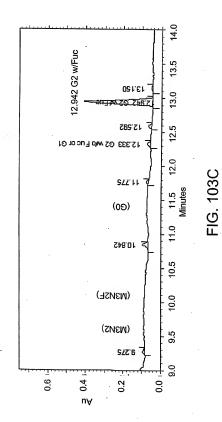


FIG. 103B



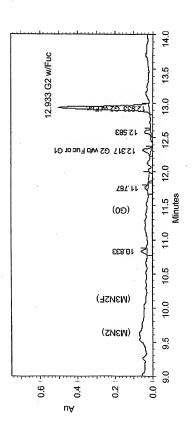
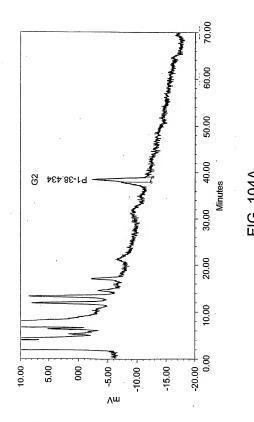


FIG. 103D



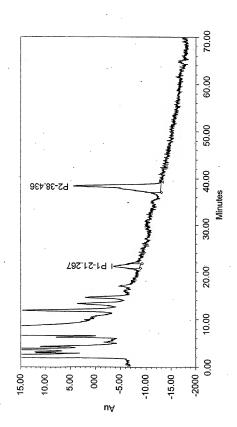


FIG. 104B

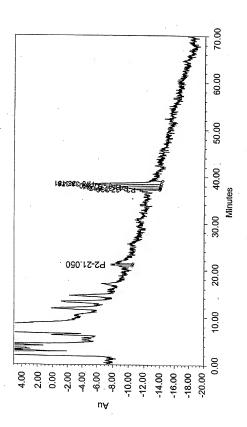


FIG. 104C

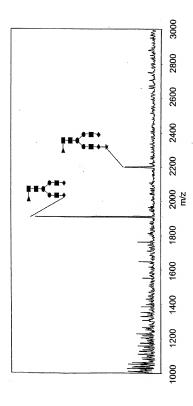


FIG. 105A

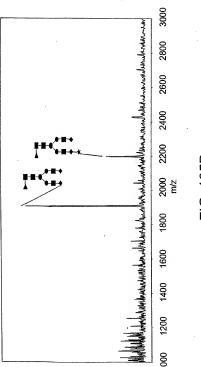


FIG. 105B

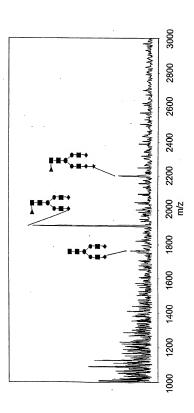
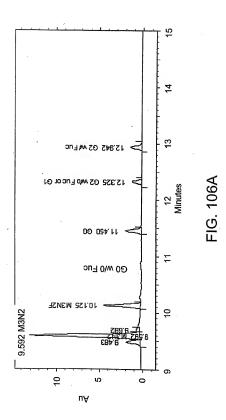
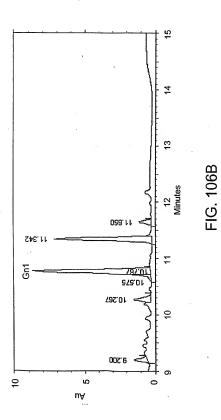
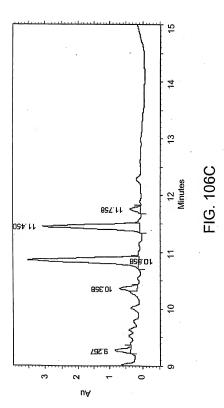
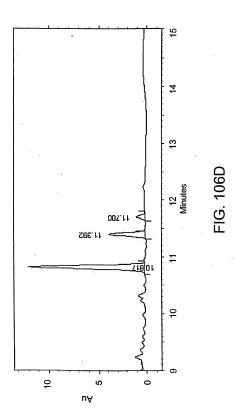


FIG. 105C









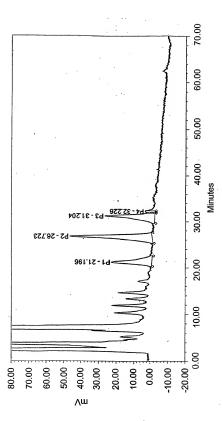
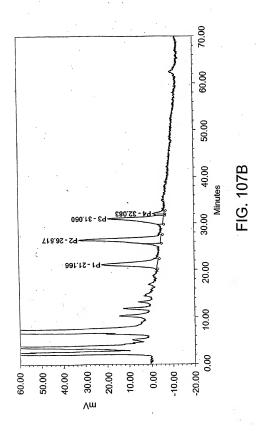


FIG. 107A



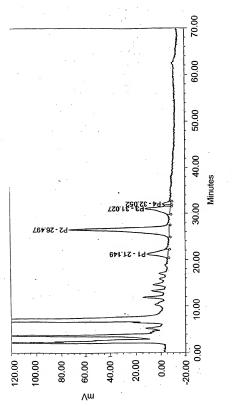
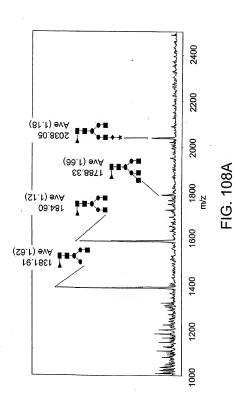


FIG. 107C



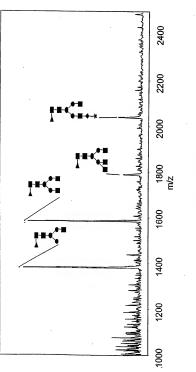


FIG. 108B

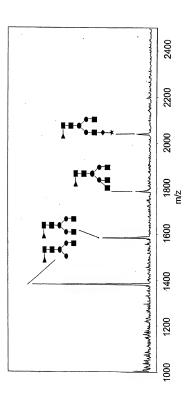
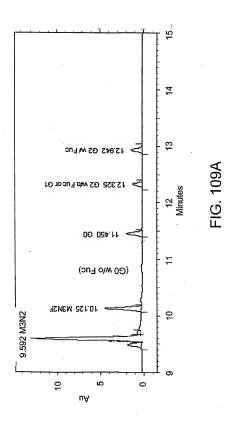
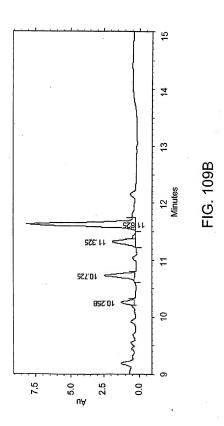
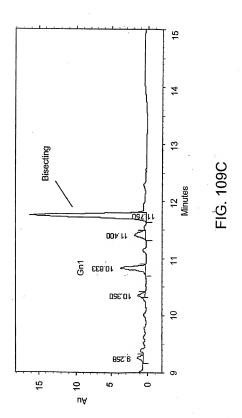


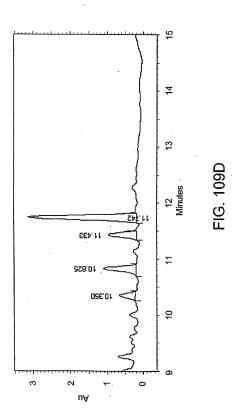
FIG. 108C

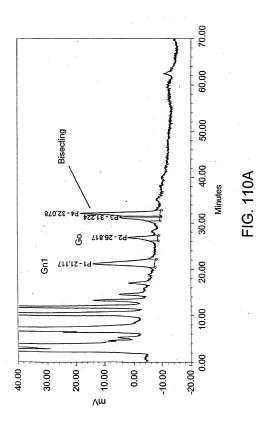
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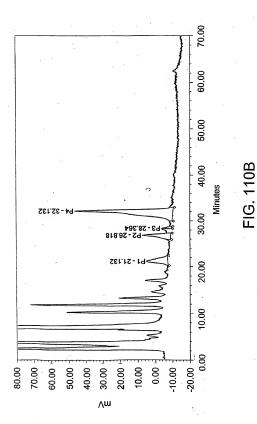


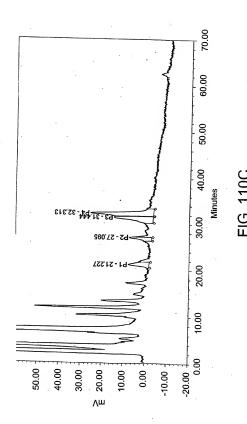




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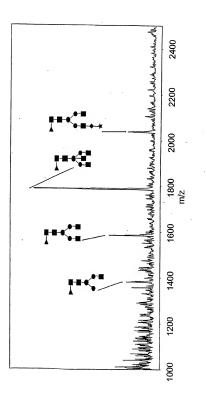


FIG. 111A

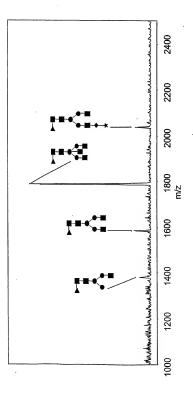


FIG. 111B

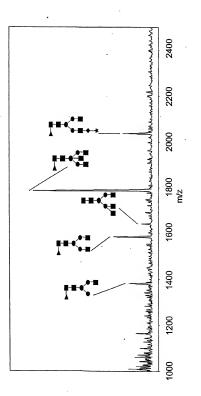


FIG. 111C

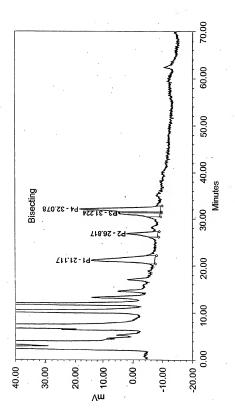
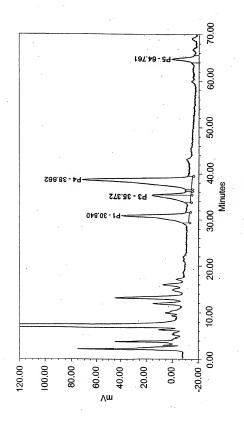
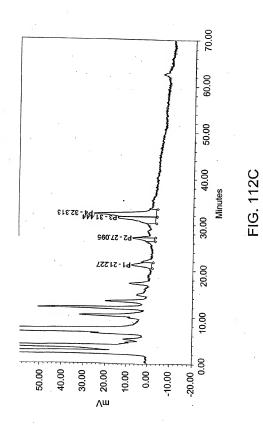
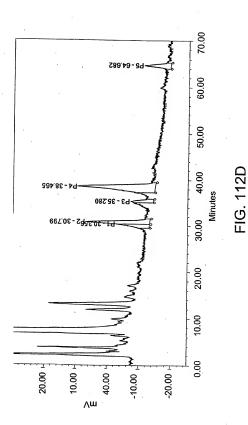


FIG. 112A



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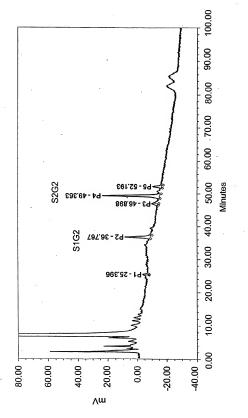
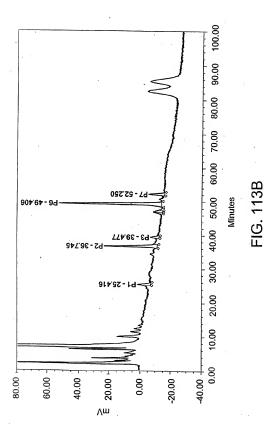
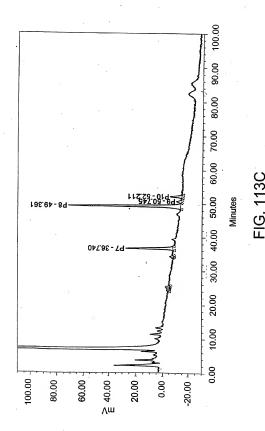
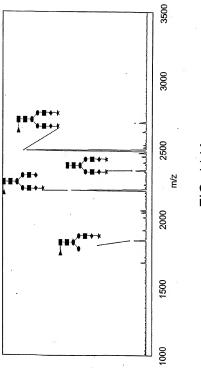


FIG. 113A







IG. 114A

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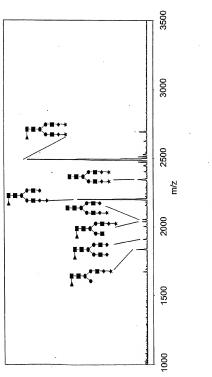
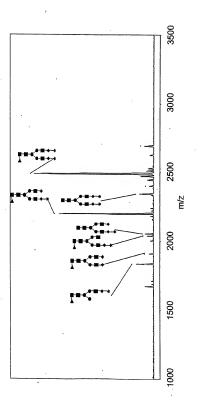


FIG. 114B

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ilg. 114C

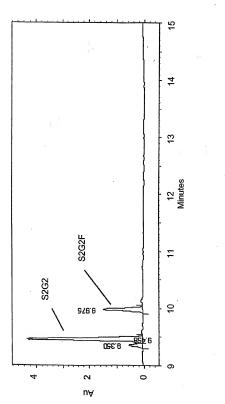
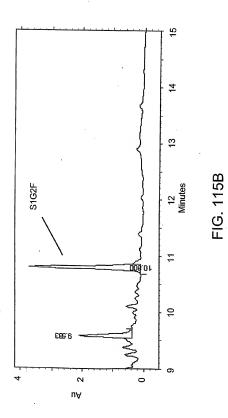
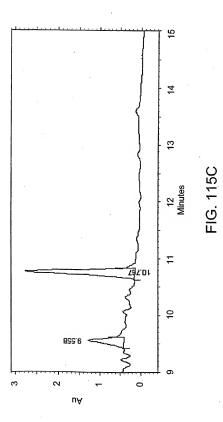


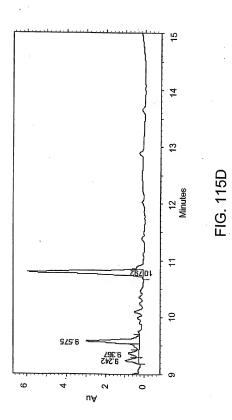
FIG. 115A

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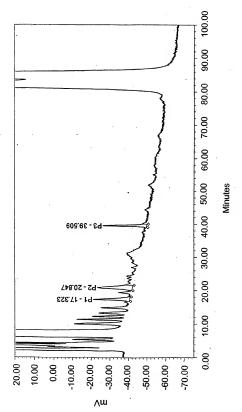


FIG. 116A

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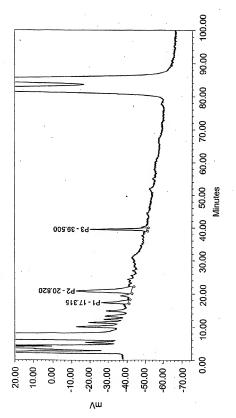


FIG. 116B

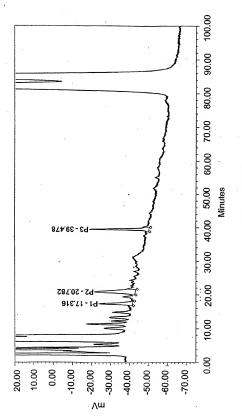


FIG. 116C

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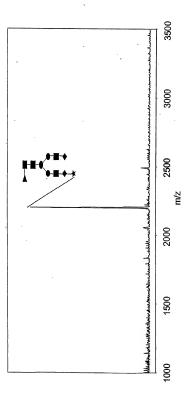
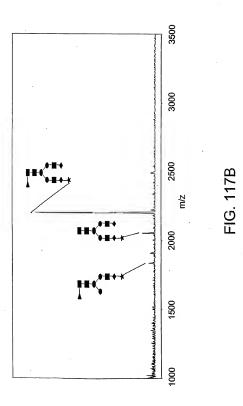


FIG. 117A

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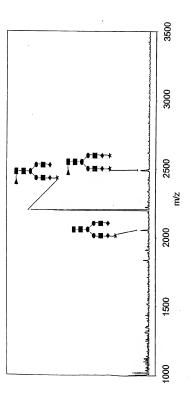
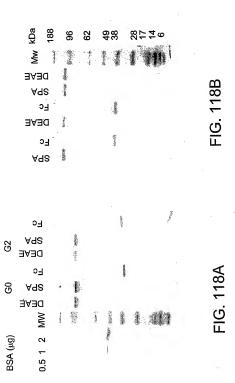


FIG. 117C



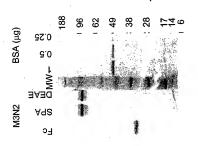


FIG. 118D



FIG. 118C

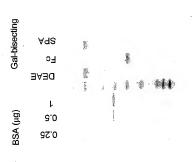
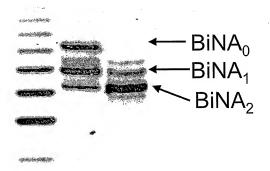


FIG. 118E

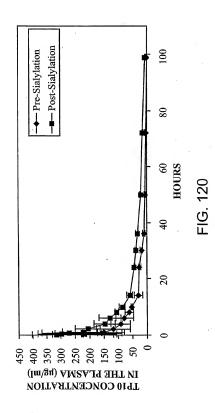
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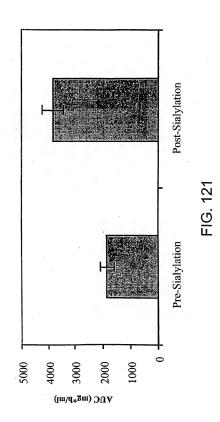


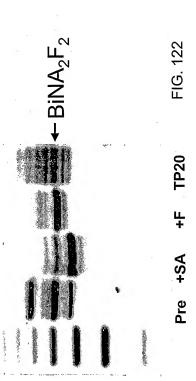
Pre Post

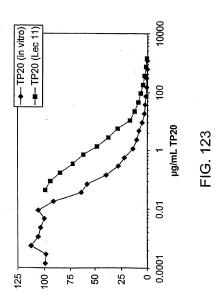
FIG. 119

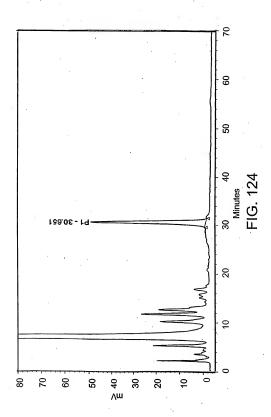


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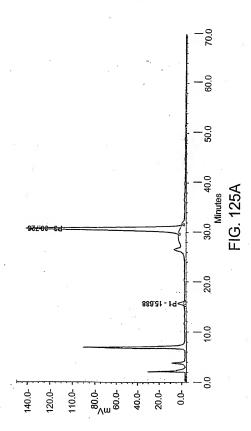




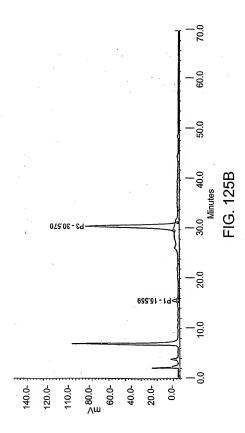


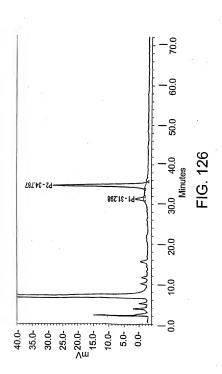


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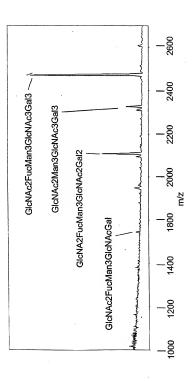


FIG. 127

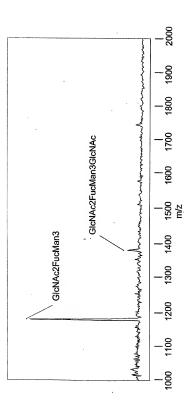


FIG. 128

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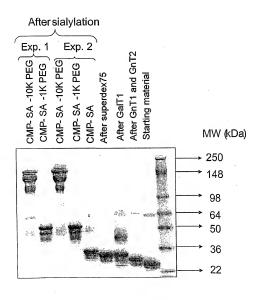


FIG. 129

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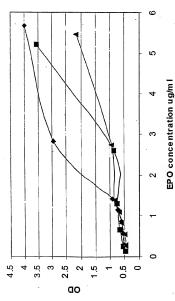
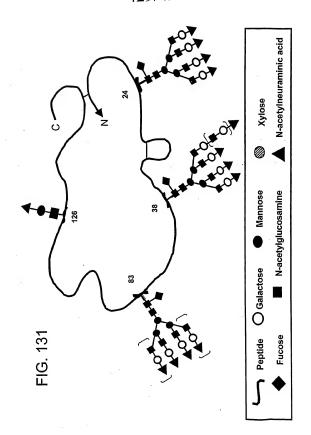
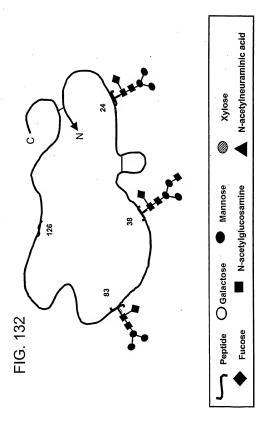


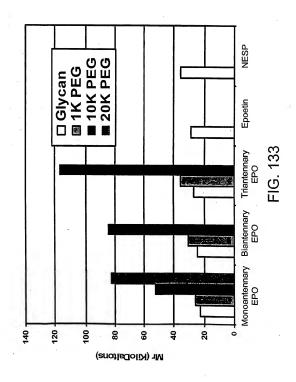
FIG. 130

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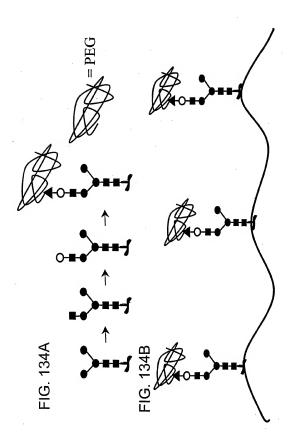


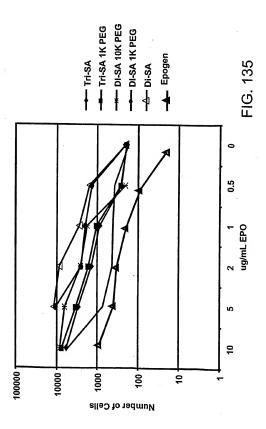
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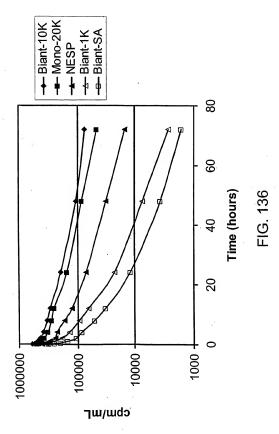


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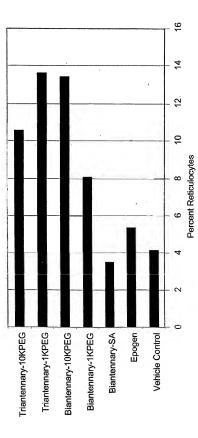


FIG. 137

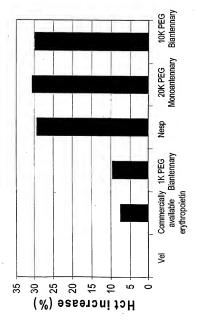
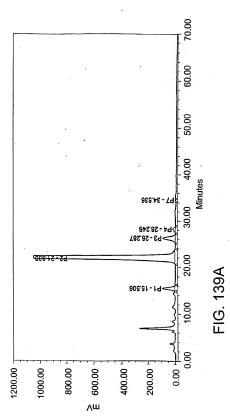


FIG. 138

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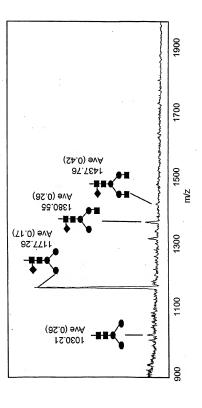


FIG. 139B

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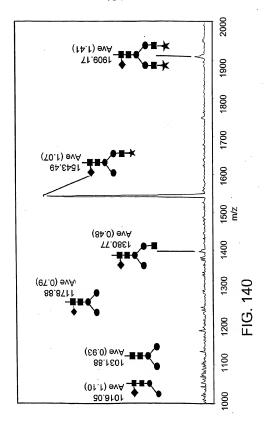
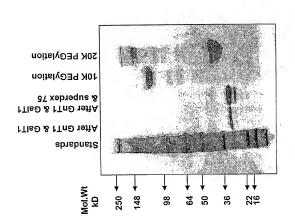


FIG. 141



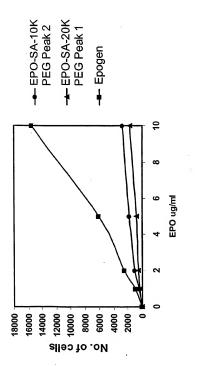


FIG. 142

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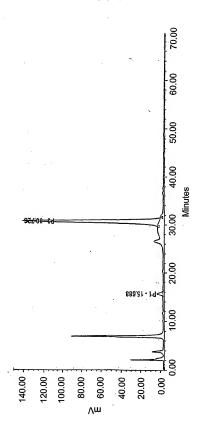


FIG. 143A

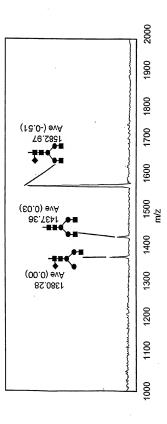


FIG. 143B

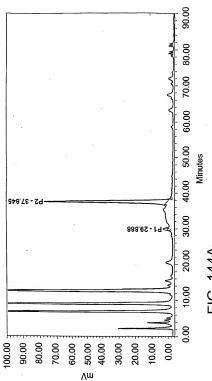


FIG. 144A

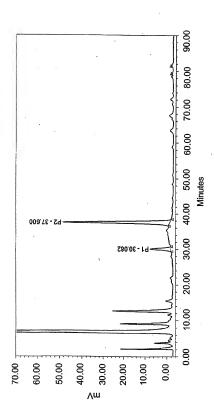


FIG. 144B

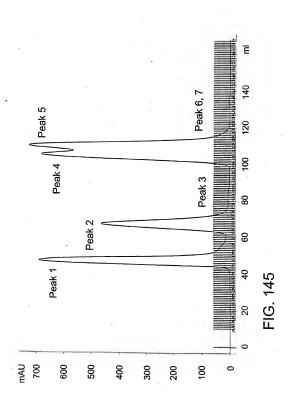
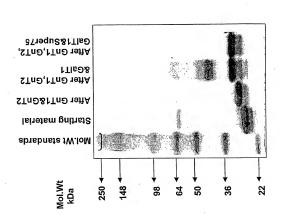
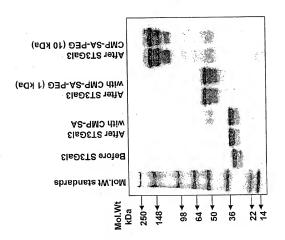


FIG. 146



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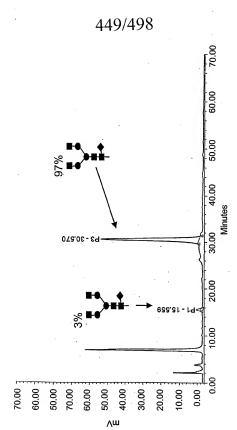
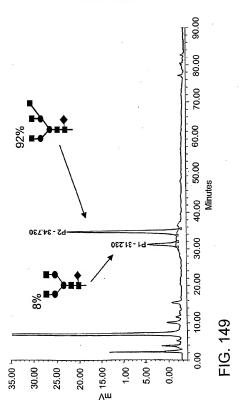
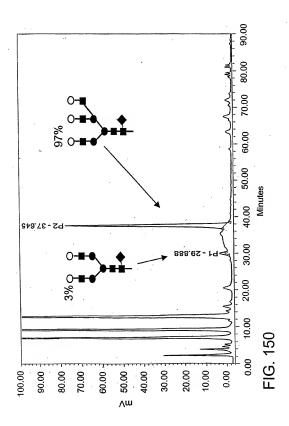
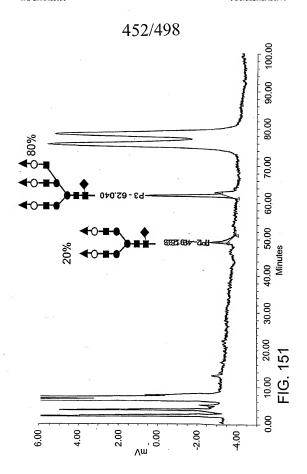


FIG. 148

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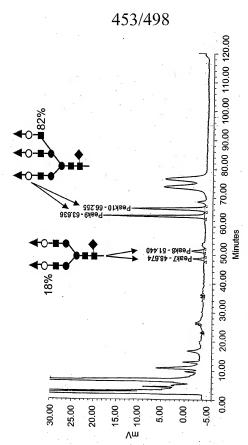
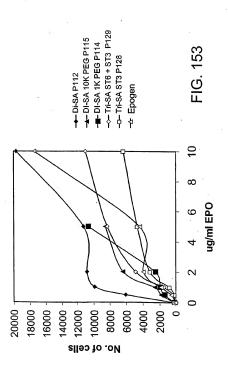


FIG. 152



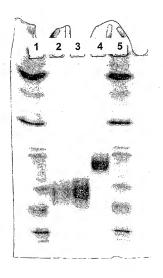


FIG. 154



FIG. 155

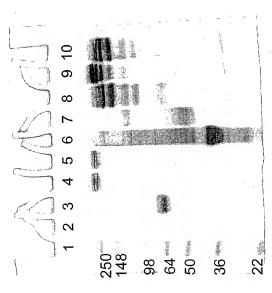


FIG. 156

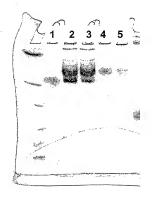
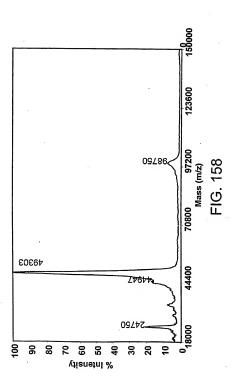
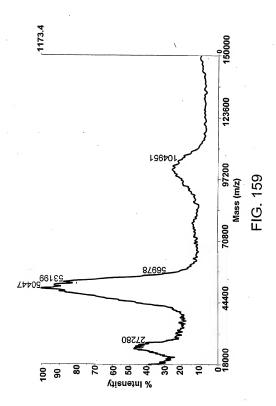
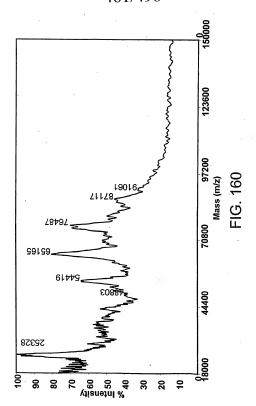


FIG. 157





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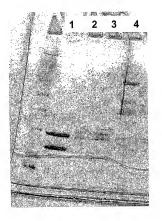


FIG. 161

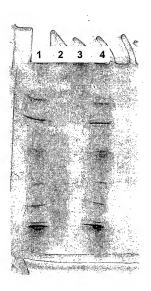


FIG. 162

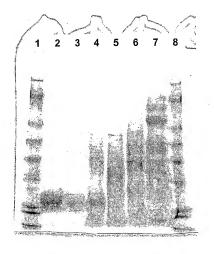


FIG. 163

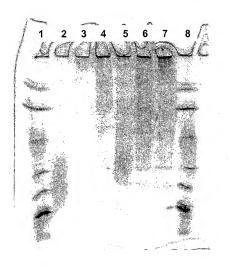


FIG. 164

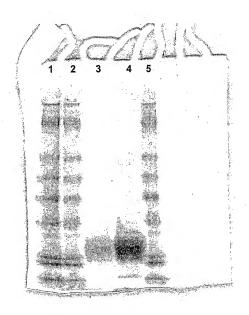


FIG. 165



FIG. 166

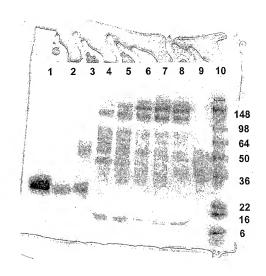


FIG. 167

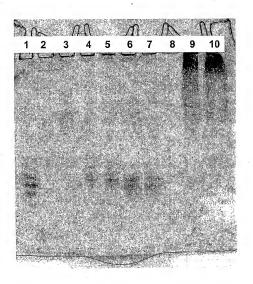
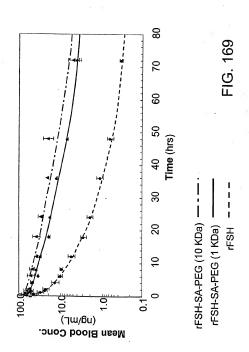


FIG. 168



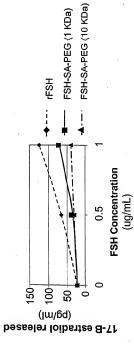
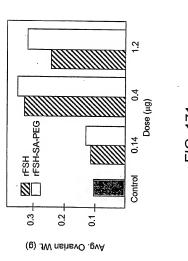
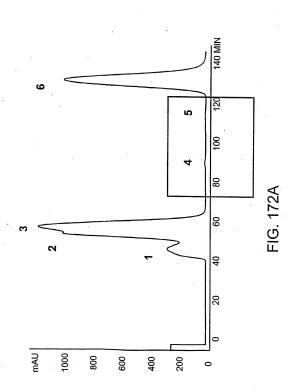


FIG. 170





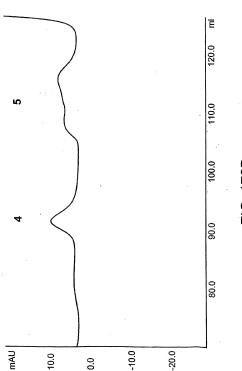
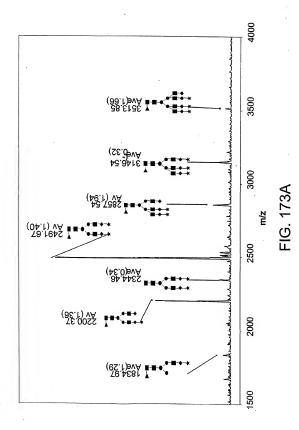


FIG 172B



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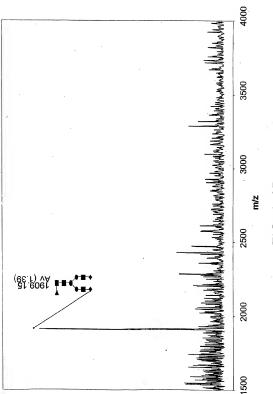


FIG. 173B

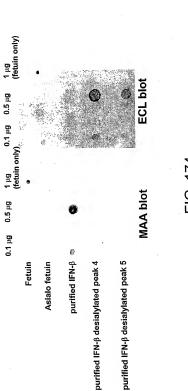
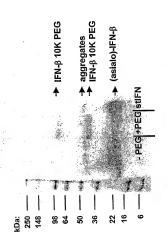
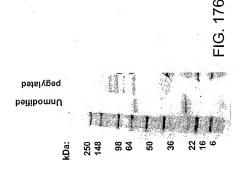


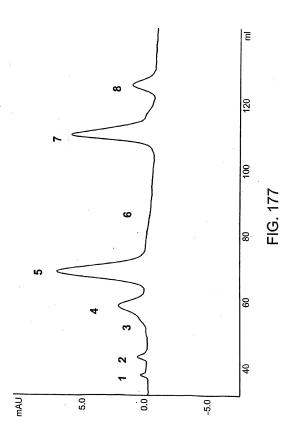
FIG. 174

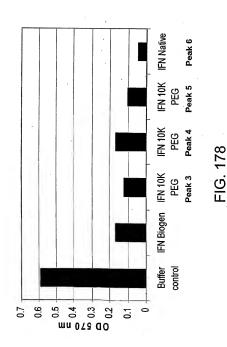


=1G. 175



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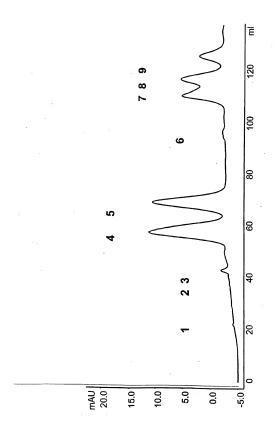
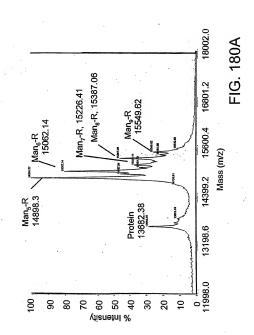
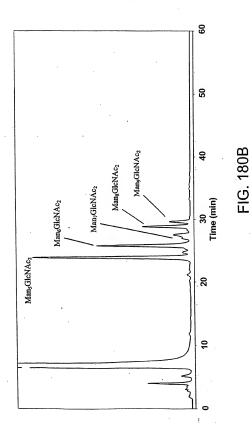


FIG. 179



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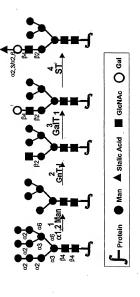


FIG. 181

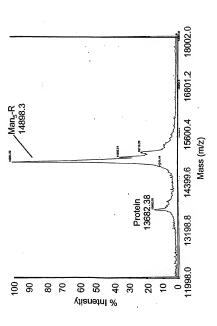
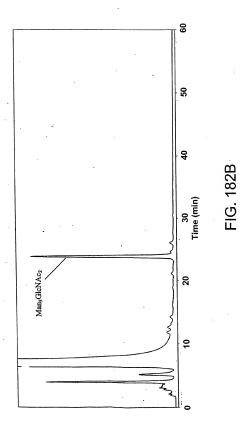
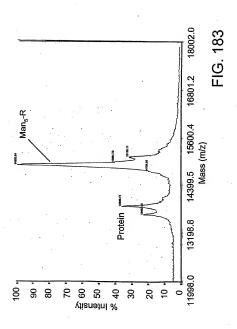
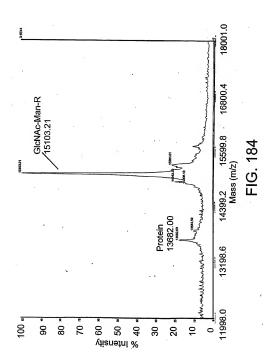


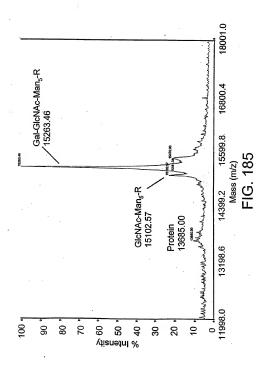
FIG. 182A

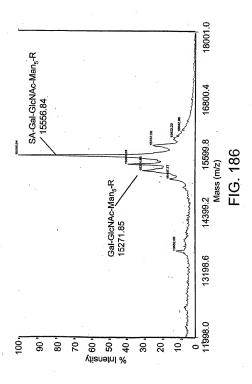
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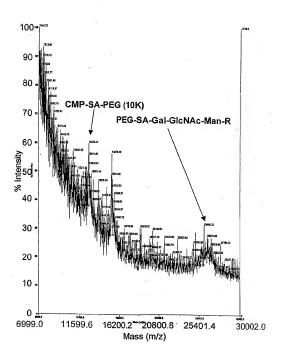


FIG. 187A

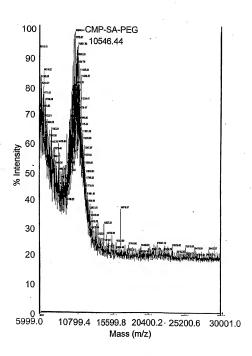
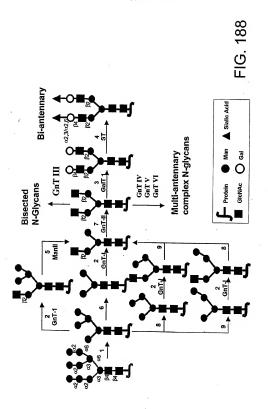


FIG. 187B



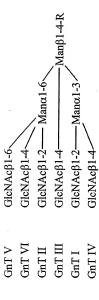


FIG. 189

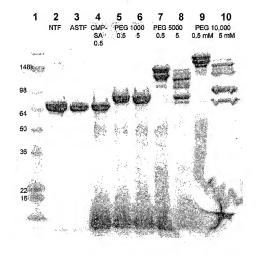


FIG. 190

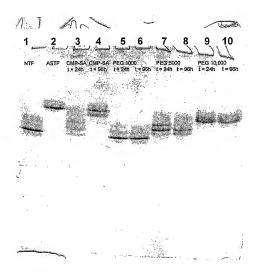
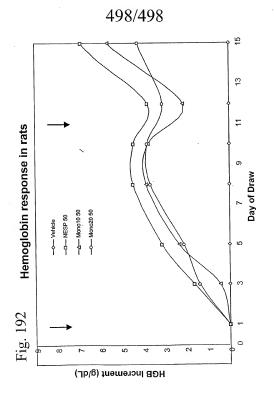


FIG. 191



#### SEQUENCE LISTING

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Phe Ala	Thr Th	r Ile	Trp	Gln	Gln 120	Met	Glu	Glu	Leu	Gly 125	Met	Ala	Pro	
Ala Leu 130	Gln Pr	o Thr	Gln	Gly 135	Ala	Met	Pro	Ala	Phe 140	Ala	Ser	Ala	Phe	
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His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser  $100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}$ 

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